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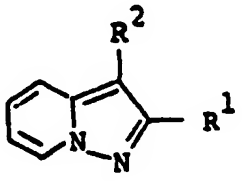
(54) Pyrazolopyridine compound and processes for preparation thereof.

(57) A pyrazolopyridine compound of the formula :



wherein
R^1 is aryl, and
R^2 is unsaturated heterocyclic group which may have one or more suitable substituent(s),
and a pharmaceutically acceptable salt thereof, processes for their preparation an pharmaceutical compositions comprising them in admixture with pharmaceutically acceptable carriers.

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PYRAZOLOPYRIDINE COMPOUND AND PROCESSES FOR PREPARATION THEREOF

The present invention relates to novel pyrazolopyridine compound and a pharmaceutically acceptable salt thereof.

More particularly, it relates to novel pyrazolopyridine compound and a pharmaceutically acceptable salt thereof, which are adenosine antagonists and possess various pharmaceutical actions such as cognitive enhancing action, analgesic action, locomotor action, antidepressant action, cerebral vasodilating action, diuretic action, cardiotonic action, vasodilating action, the action of increasing the renal blood flow, enhanced lipolysis action, inhibited anaphylactic bronchoconstrictive action, accelerating action of the release of insulin, or the like, and so are useful as psychostimulant, analgesic, antidepressant, ameliorants of cerebral circulation, remedy for heart failure, cardiotonic agent, antihypertensive agent, remedy for renal insufficiency, diuretic, remedy for edema, antiobesity, antiasthmatic, bronchoconstrictor, remedy for apnea, remedy for gout, remedy for hyperuricemia, remedy for sudden infant death syndrome (SIDS), ameliorants of immunosuppresion action of adenosine, antidiabetic agent, or the like, and further which are inhibitors of platelet aggregation, so are useful as remedy for thrombosis, remedy for myocardiac infarction, remedy for obstruction, remedy for arteriosclerosis obliterans, remedy for thrombophlebitis, remedy for cerebral infarction, remedy for transient ischemic attack, remedy for angina pectoris, or the like; to a process for preparation thereof, to a pharmaceutical composition comprising the same, and to a method for using the same therapeutically in human being and animals for the treatment of melancholia, heart failure, hypertension (e.g. essential hypertension, nephrogenous hypertension, etc.), renal insufficiency, edema (e.g. cardiac edema, nephrotic edema, hepatic edema, idiopathic edema, drug edema, acute angioneurotic edema, hereditary angioneurotic edema, carcionomatous ascites, gestational edema, etc.), obesity, bronchial asthma, gout, hyperuricemia, sudden infant death syndrome, immunosuppresion, diabetes, myocardiac infarction, thrombosis (e.g. arterial thrombosis, cerebral thrombosis, etc.), obstruction, arteriosclerosis obliterans, thrombophlebitis, cerebral infarction, transient ischemic attack, angina pectoris or the like.

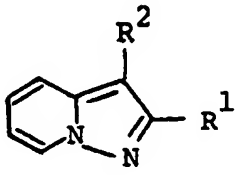
Accordingly, one object of the present invention is to provide the novel pyrazolopyridine compound and a pharmaceutically acceptable salt thereof, which are useful as stated above.

Another object of the present invention is to provide processes for the preparation of the novel pyrazolopyridine compound or a salt thereof.

A further object of the present invention is to provide a pharmaceutical composition comprising, as an active ingredient, said pyrazolopyridine compound or a pharmaceutically acceptable salt thereof.

Still further object of the present invention is to provide a method for using said pyrazolopyridine compound as aforesaid therapeutic use, which comprises administering said pyrazolopyridine compound to human being or animals.

The novel pyrazolopyridine compound of the present invention can be shown by the following formula (I).



(I)

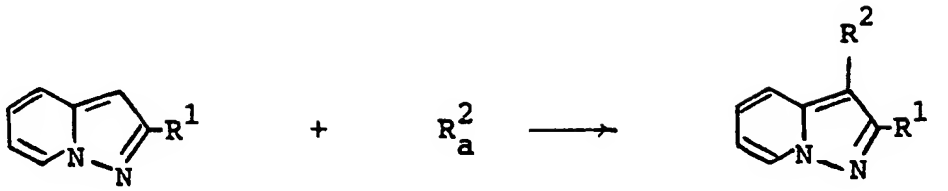
wherein

R^1 is aryl, and

R^2 is unsaturated heterocyclic group which may have one or more suitable substituent(s).

The object compound (I) or a salt thereof can be prepared, for example, according to the following reaction schemes.

Process 1

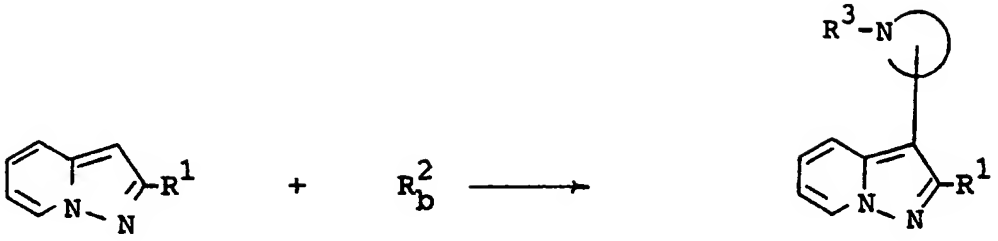


(II) or a salt thereof

(III) or a salt thereof

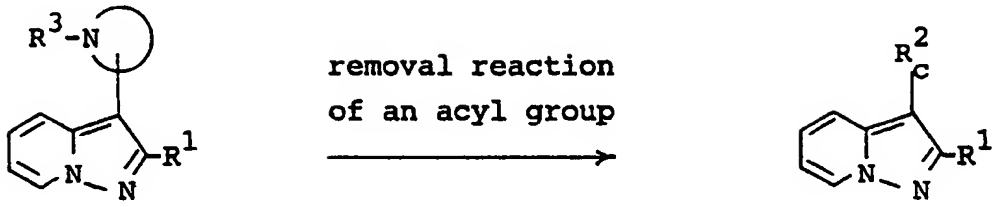
(I) or a salt thereof

Process 2



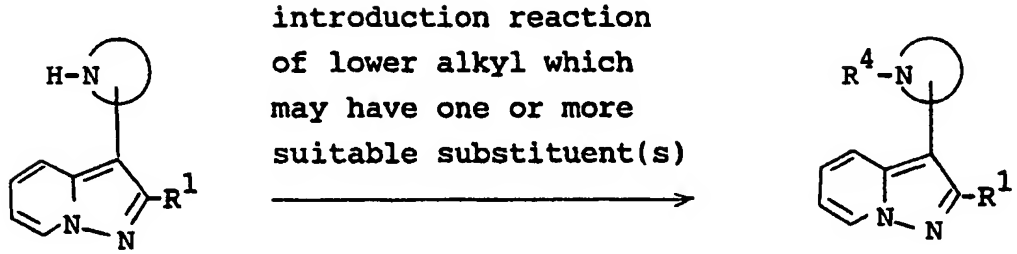
(II) or a salt thereof + (IV) or a salt thereof → (Ia) or a salt thereof

Process 3



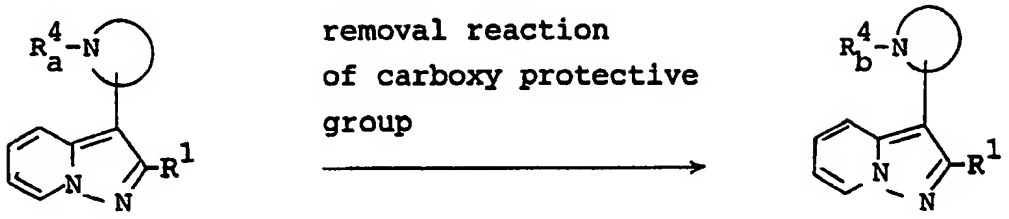
(Ia) or a salt thereof → (Ib) or a salt thereof

Process 4



(Ic) or a salt thereof → (Id) or a salt thereof

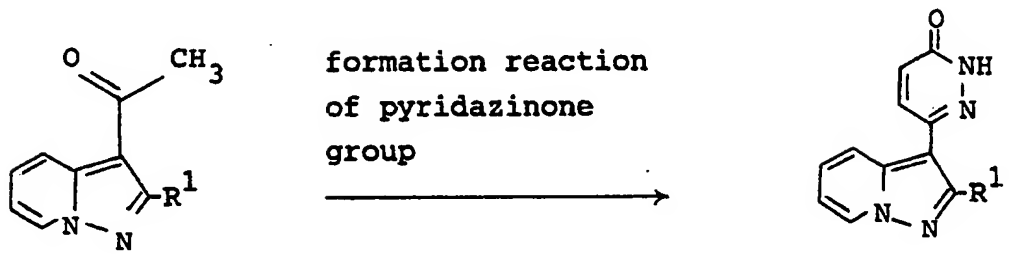
Process 5



(Ie)
or a salt thereof

(If)
or a salt thereof

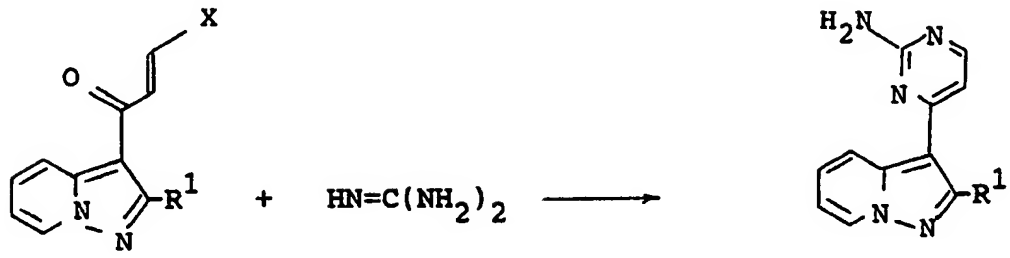
Process 6



(V)
or a salt thereof

(Ig)
or a salt thereof

Process 7

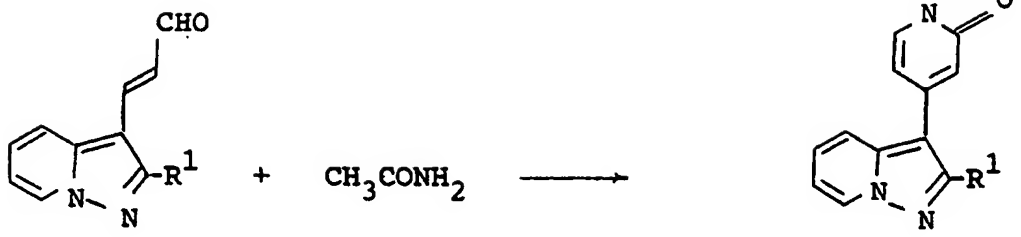


(VI)
or a salt thereof

(VII)
or a salt therof

(Ih)
or a salt thereof

Process 8

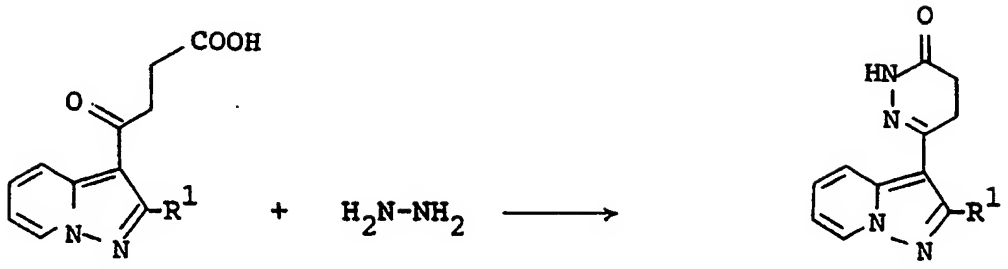


(VIII) or a salt thereof

(IX) or its reactive derivative at methyl group or a salt thereof

(Ii) or a salt thereof

Process 9

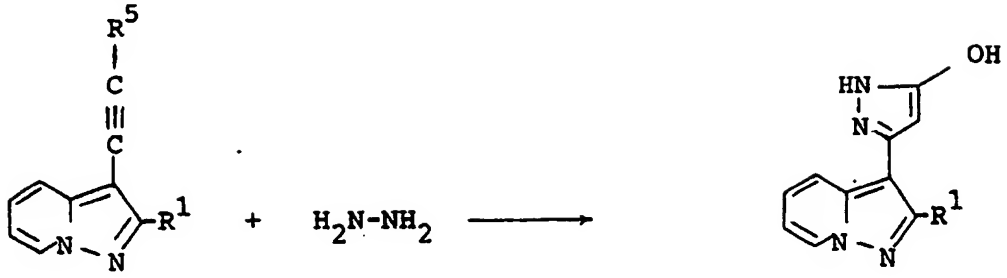


(X) or a salt thereof

(XI) or a salt thereof

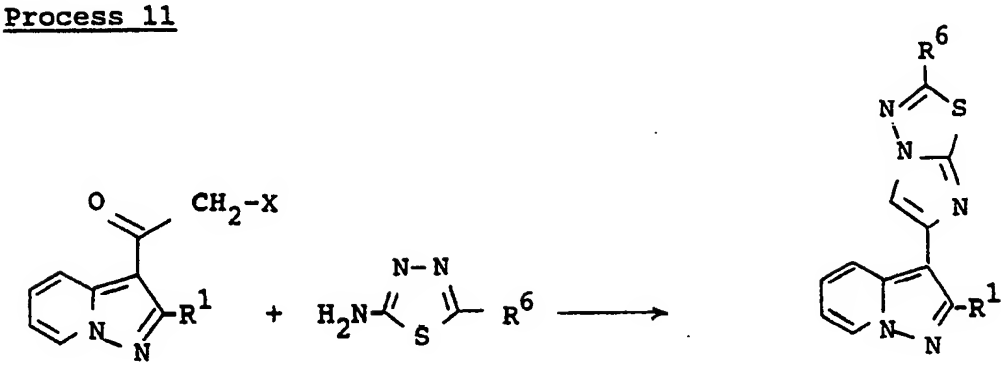
(Ij) or a salt thereof

Process 10



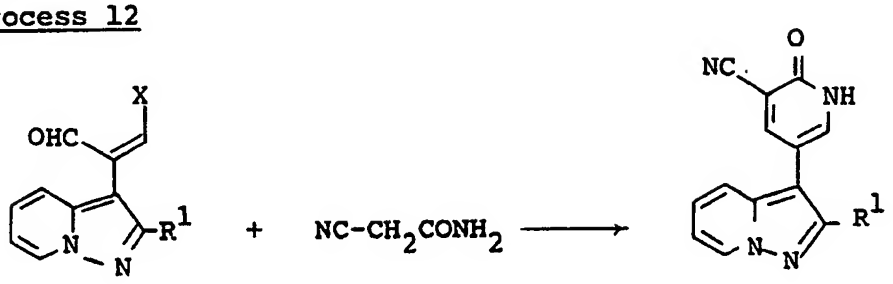
(XII) or a salt thereof + (XI) or a salt thereof → (Ik) or a salt thereof

Process 11



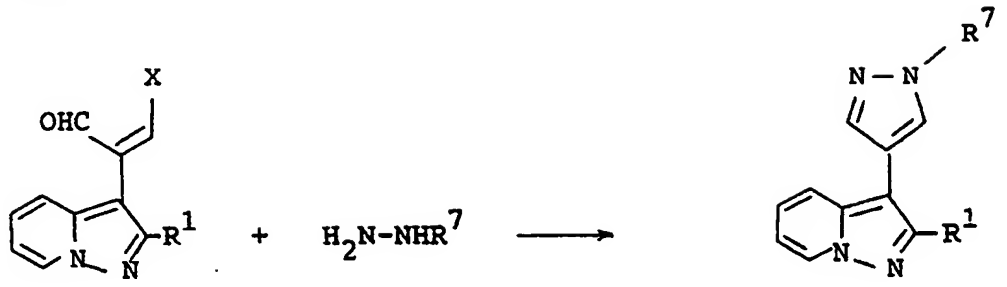
(XIII) or a salt thereof + (XIV) or a salt therof → (Il) or a salt thereof

Process 12



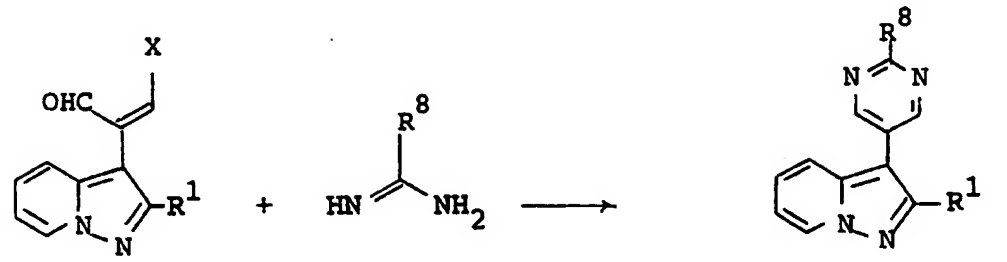
(XV) or a salt thereof + (XVI) or a salt thereof → (Im) or a salt thereof

Process 13



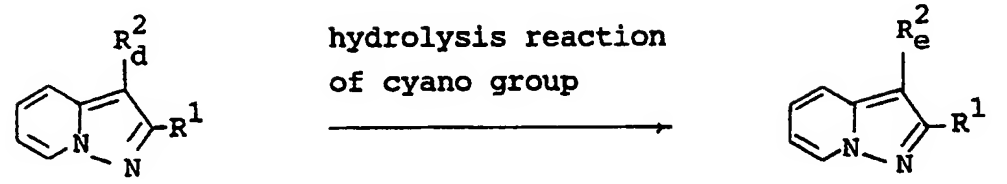
(XV) or a salt thereof + (XVII) or a salt thereof → (In) or a salt thereof

Process 14



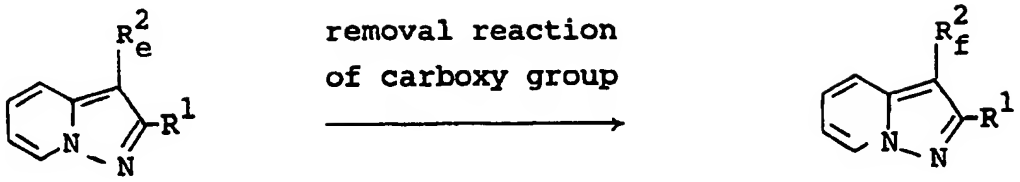
(XV) or a salt thereof + (XVIII) or a salt thereof → (Io) or a salt thereof

Process 15



(Ip) or a salt thereof → (Iq) or a salt thereof

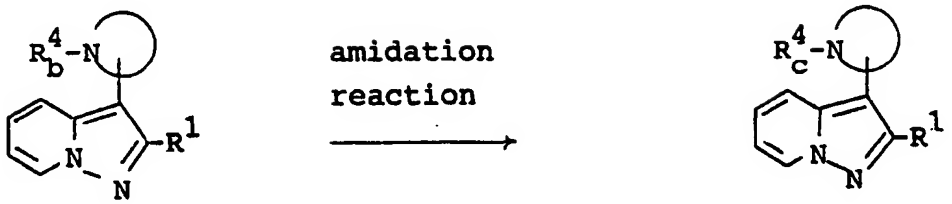
Process 16



(Iq)
or a salt thereof

(Ir)
or a salt thereof

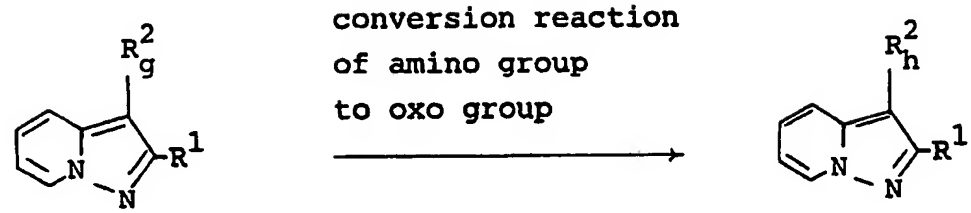
Process 17



(If)
or a salt thereof

(Is)
or a salt thereof

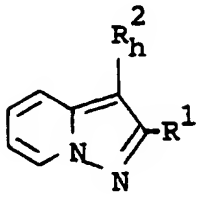
Process 18



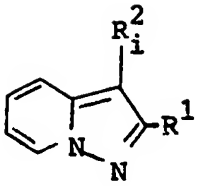
(It)
or a salt thereof

(Iu)
or a salt thereof

Process 19



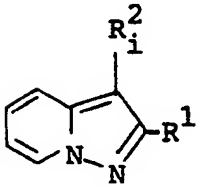
halogenation reaction



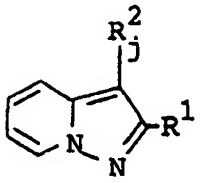
(Iu) or a salt thereof

(Iv) or a salt thereof

Process 20



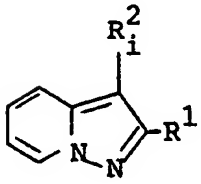
di(lower)alkylamine (XIX) or a salt thereof



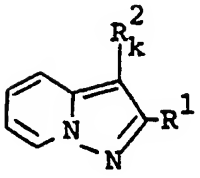
(Iv) or a salt thereof

(Iw) or a salt thereof

Process 21



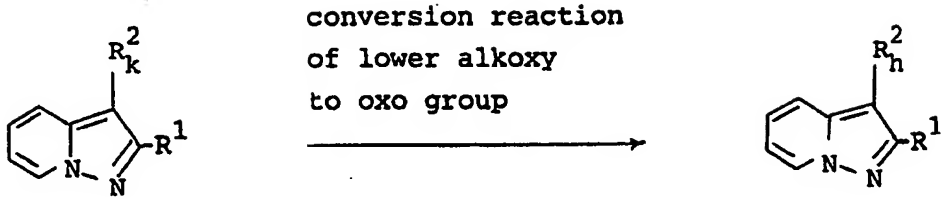
conversion reaction of halogen to lower alkoxy



(Iv) or a salt thereof

(Ix) or a salt thereof

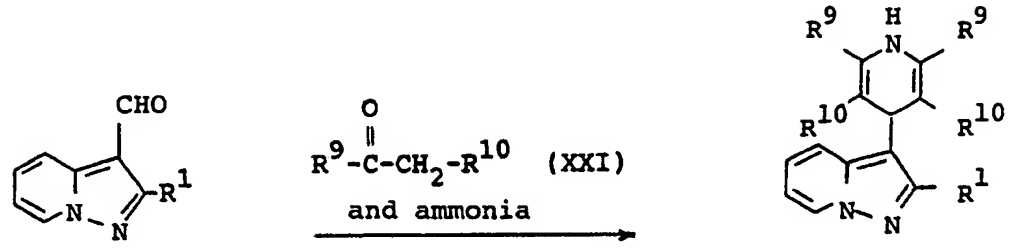
Process 22



(Ix)
or a salt thereof

(Iv)
or a salt thereof

Process 23

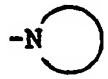


(XX)
or a salt thereof

(Iy)
or a salt thereof

wherein
R^1 and R^2 are each as defined above,
R^2_a is heterocyclic compound having

moiety in its ring, which may have one or more suitable substituent(s),
R^2_b is N-containing unsaturated heterocyclic compound having =N- moiety in its ring, which may have one or more suitable substituent(s),
R^2_c is N-containing unsaturated heterocyclic group, which may have one or more suitable substituent(s),
R^2_d is unsaturated heterocyclic group having cyano, which may have one or more suitable substituent(s),
R^2_e is unsaturated heterocyclic group having carboxy, which may have one or more suitable substituent(s),
R^2_f is unsaturated heterocyclic group which may have one or more suitable substituent(s) except carboxy,
R^2_g is unsaturated heterocyclic group having amino, which may have one or more suitable substituent(s),
R^2_h is unsaturated heterocyclic group having oxo, which may have one or more suitable substituent(s),
R^2_i is unsaturated heterocyclic group having halogen, which may have one or more suitable substituent(s),
R^2_j is unsaturated heterocyclic group having di(lower)alkylamino, which may have one or more suitable substituent(s),
R^2_k is unsaturated heterocyclic group having lower alkoxy, which may have one or more suitable substituent-(s),
a group of the formula :



is unsaturated cyclic amino group, which may have one or more suitable substituent(s),
R^3 is an acyl group,
R^4 is lower alkyl which may have one or more suitable substituent(s),
R^4_a is protected carboxy(lower)alkyl,
R^4_b is carboxy(lower)alkyl,
R^4_c is amidated carboxy(lower)alkyl,
R^5 is protected carboxy,
R^6 is lower alkyl,
R^7 is hydrogen or lower alkyl,
R^8 is hydrogen, lower alkyl or amino,
R^9 is lower alkyl,
R^{10} is protected carboxy,
X is a leaving group.

Among the starting compounds, the compounds (VI), (X), (XII) and (XV) are novel, and they can be prepared according to the methods described in Preparations disclosed later in the present specification or similar manners thereto.

Suitable pharmaceutically acceptable salts of the object compound (I) are conventional ones and include a metal salt such as an alkali metal salt (e.g. sodium salt, potassium salt, etc.) and an alkaline earth metal salt (e.g. calcium salt, magnesium salt, etc.), an ammonium salt, an organic base salt (e.g. trimethylamine salt, triethylamine salt, pyridine salt, picoline salt, dicyclohexylamine salt, N,N'-dibenzylethylenediamine salt, etc.), an organic acid salt (e.g. acetate, trifluoroacetate, maleate, tartrate, fumalate, methanesulfonate, benzenesulfonate, formate, toluenesulfonate, etc.), an inorganic acid salt (e.g. hydrochloride, hydrobromide, hydroiodide, sulfate, phosphate, etc.), a salt with an amino acid (e.g. arginine, aspartic acid, glutamic acid, etc.), and the like.

In the above and following descriptions of the present specification, suitable examples and illustrations of the various definitions which the present invention includes within the scope thereof are explained in detail as follows.

The term "lower" is intended to mean 1 to 6 carbon atom(s) unless otherwise indicated.

Suitable "aryl" may include phenyl, tolyl, xylyl, naphthyl and the like, in which the preferred one may be phenyl.

Suitable "unsaturated heterocyclic group" may include unsaturated, monocyclic or polycyclic heterocyclic group containing at least one hetero atom such as nitrogen, oxygen, sulfur or the like.

Suitable examples of said "unsaturated heterocyclic group" may include :
unsaturated 3 to 8-membered (more preferably 5 to 7-membered) heteromonocyclic group containing 1 to 4 nitrogen atom(s), for example, azepinyl (e.g. 1H-azepinyl, etc.) pyrrolyl, pyrrolinyl, imidazolyl, pyrazolyl, pyridyl, dihydropyridyl (e.g. 1,2-dihydropyridyl, 1,4-dihydropyridyl, etc.), tetrahydropyridyl (e.g. 1,2,3,6-tetrahydropyridyl, etc.) pyrimidinyl, dihydropyrimidinyl (e.g. 1,2-dihydropyrimidinyl, etc.), pyrazinyl, pyridazinyl, dihydropyridazinyl (e.g. 2,3-dihydropyridazinyl, 1,4-dihydropyridazinyl, etc.), tetrahydropyridazinyl (e.g. 2,3,4,5-tetrahydropyridazinyl, etc.) triazolyl (e.g. 4H-1,2,4-triazolyl, 1H-1,2,3-triazolyl, 2H-1,2,3-triazolyl, etc.), tetrazolyl (e.g. 1H-tetrazolyl, 2H-tetrazolyl, etc.), etc.;
unsaturated condensed heterocyclic group containing 1 to 4 nitrogen atom(s), for example, indolyl, isoindolyl, indolizinyl, benzimidazolyl, quinolyl, dihydroquinolyl (e.g. 2,3-dihydroquinolyl, etc.) isoquinolyl, indazolyl, benzotriazolyl, etc.;
unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing 1 to 2 oxygen atom(s) and 1 to 3 nitrogen atom(s), for example, oxazolyl, isoxazolyl, dihydroisoxazolyl (e.g. 2,5-dihydroisoxazolyl, etc.) oxadiazolyl (e.g. 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,5-oxadiazolyl, etc.), etc.;
unsaturated condensed heterocyclic group containing 1 to 2 oxygen atom(s) and 1 to 3 nitrogen atom(s), for example, benzoxazolyl, benzoxadiazolyl, etc.;
unsaturated 3 to 8-membered (more preferably 5 or 6-membered)heteromonocyclic group containing 1 to 2 sulfur atom(s) and 1 to 3 nitrogen atom(s), for example, thiazolyl, dihydrothiazolyl (e.g. 2,3-dihydrothiazolyl, etc.) isothiazolyl, thiadiazolyl (e.g. 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,5-thiadiazolyl, etc.), dihydrothiazinyl, etc.;
unsaturated condensed heterocyclic group containing 1 to 2 sulfur atom(s) and 1 to 3 nitrogen atom(s), for example, benzothiazolyl, benzothiadiazolyl, (e.g. benzo[d][1,2,3]thiadiazolyl, etc.), imidazothiadiazolyl (e.g. 5H-imidazo[2,1-b][1,3,4]thiadiazolyl, etc.), etc.;
unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing 1 to 2 sulfur atom(s), for example, thienyl, dihydrodithiinyl, etc.;
unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing an

oxygen atom, for example, furyl, etc.;
unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing an oxygen atom and 1 to 2 sulfur atom(s), for example, dihydrooxathiinyl, etc.;
unsaturated condensed heterocyclic group containing 1 to 2 sulfur atom(s), for example, benzothienyl, benzodithiinyl, etc.;
unsaturated condensed heterocyclic group containing an oxygen atom and 1 to 2 sulfur atom(s) for example, benzoxathiinyl, etc. and the like, in which the preferred one may be unsaturated heterocyclic group containing at least one nitrogen atom as hetero atom, the more preferred one may be unsaturated 3 to 8-membered heteromonocyclic group containing 1 to 4 nitrogen atom(s) and unsaturated condensed heterocyclic group containing 1 to 2 sulfur atom(s) and 1 to 3 nitrogen atom(s), the much more preferred one may be pyridazinyl, dihydropyridazinyl, tetrahydropyridazinyl, pyrimidinyl, dihydropyrimidinyl, pyridyl, dihydropyridyl, tetrahydropyridyl, pyrazolyl and imidazothiadiazolyl, and the most preferred one may be pyridazinyl, 2,3-dihydropyridazinyl, 1,4-dihydropyridazinyl, 2,3,4,5-tetrahydropyridazinyl, pyrimidinyl, 1,2-dihydropyrimidinyl, pyridyl, 1,2-dihydropyridyl, 1,4-dihydropyridyl, 1,2,3,6-tetrahydropyridyl, pyrazolyl, and imidazo[2,1-b][1,3,4]thiadiazolyl.

Aforesaid "unsaturated heterocyclic group" may have one or more (preferably 1 to 4) suitable substituent(s) such as lower alkyl (e.g. methyl, ethyl, propyl, isopropyl, butyl, t-butyl, pentyl, hexyl, etc.) which may have one or more (preferably 1 to 4) suitable substituent(s) as explained below; carboxy(lower)-alkenyl (e.g. 1-carboxyvinyl, 2-carboxyvinyl, 1-carboxy-2-propenyl, 3-carboxy-2-propenyl, 3-carboxy-2-butenyl, 4-carboxy-2-methyl-2-butenyl, 3-carboxy-1-hexenyl, etc.); amino; di-lower)alkylamino (e.g. dimethylamino, N-methylethylamino, dipropylamino, N-butyl-(2-methylbutyl)amino, N-pentylhexylamino, etc.); halogen (e.g. fluoro, chloro, bromo, iodo, etc.); lower alkoxy (e.g. methoxy, ethoxy, propoxy, isopropoxy, butoxy, t-butoxy, pentyloxy, hexyloxy, etc.); oxo; hydroxy; cyano; an acyl group as explained below; or the like.

Suitable "an acyl group" may include lower alkanoyl (e.g. formyl, acetyl, propionyl, butyryl, isobutyryl, pivaloyl, hexanoyl, etc.), carboxy, protected carboxy, and the like.

Suitable examples of aforesaid "protected carboxy" may be esterified carboxy, in which suitable esterified carboxy may include lower alkoxycarbonyl (e.g. methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, t-butoxycarbonyl, pentyloxycarbonyl, hexyloxycarbonyl, etc.) and the like;
amidated carboxy, in which suitable amidated carboxy may include carbamoyl, N,N-di-lower)alkylcarbamoyl wherein two lower alkyl groups may bond to each other to form 3 to 6-membered ring (e.g. N,N-dimethylcarbamoyl, N-methyl-N-ethylcarbamoyl, N,N-diethylcarbamoyl, N,N-dipropylcarbamoyl, N-butyl-N-t-butylcarbamoyl, N,N-dipentylcarbamoyl, N-pentyl-N-hexylcarbamoyl, 1-aziridinylcarbonyl, 1-azetidinylcarbonyl, 1-pyrrolidinylcarbonyl, piperidinocarbonyl, etc.) and the like; or the like.

Suitable examples of "suitable substituent(s)" of aforesaid "lower alkyl which may have one or more suitable substituent(s)" may include hydroxy, aforesaid halogen, aforesaid lower alkoxy, aforesaid an acyl group, and the like.

Suitable examples of said "lower alkyl having one or more suitable substituent(s)" may include lower alkyl having hydroxy and halogen (e.g. 1-hydroxy-1-chloromethyl, 1-hydroxy-2-chloroethyl, 2-hydroxy-3-fluoropropyl, 2-hydroxy-3,3,3-trichloropropyl, 3-bromo-4-hydroxy-4-iodobutyl, 1-chloro-2-hydroxy-4-fluoropentyl, 3,4-dihydroxy-6-chlorohexyl, etc);
hydroxy-lower)alkyl (e.g. hydroxymethyl, 2-hydroxyethyl, 2-hydroxypropyl, 3-hydroxypropyl, 1-hydroxy-1-methylethyl, 1-hydroxybutyl, 1-hydroxymethyl-1-methylethyl, 3-hydroxypentyl, 2-hydroxyhexyl, etc.);
lower alkoxy(lower)alkyl (e.g. methoxymethyl, ethoxymethyl, 2-ethoxyethyl, 1-propoxyethyl, 3-isopropoxypropyl, 2-butoxybutyl, 1-t-butoxymethyl-1-methylethyl, 5-pentyloxypentyl, hexyloxymethyl, 3-hexyloxyhexyl, etc.);
acyl(lower)alkyl, in which the preferred one may be carboxy(lower)alkyl (e.g. carboxymethyl, 2-carboxyethyl, 2-carboxypropyl, 3-carboxypropyl, 2-carboxy-1-methylethyl, 4-carboxybutyl, 1-carboxymethyl-1-methylethyl, 3-carboxypentyl, 2-carboxyhexyl, etc.), and protected carboxy(lower)alkyl, in which the preferred one may be esterified carboxy-lower)alkyl and amidated carboxy-lower)alkyl, the more preferred one may be lower alkoxycarbonyl-lower)alkyl (e.g. methoxycarbonylmethyl, ethoxycarbonylmethyl, 2-methoxycarbonylethyl, 2-ethoxycarbonylethyl, 1-propoxycarbonylethyl, 3-ethoxycarbonylpropyl, 2-butoxycarbonylbutyl, 4-ethoxycarbonylbutyl, 1-t-butoxycarbonylmethyl-1-methylethyl, 5-pentyloxycarbonylpentyl, hexyloxycarbonylmethyl, 3-hexyloxycarbonylhexyl, etc.), carbamoyl(lower)alkyl (e.g. carbamoylmethyl, 2-carbamoylethyl, 3-carbamoylpropyl, 2-carbamoyl-1-methylethyl, 4-carbamoylbutyl, 1-carbamoylmethyl-1-methylethyl, 5-carbamoylpentyl, 3-carbamoylhexyl, etc.), N,N-di(lower)alkylcarbamoyl(lower)alkyl in which two lower alkyl groups on nitrogen atom may bond to each other to form 3 to 6-membered ring [e.g. N,N-dimethylcarbamoylmethyl, 2-(N,N-dimethylcarbamoyl)ethyl, 2-(N-methyl-N-ethylcarbamoyl)ethyl, 3-(N-methyl-N-ethylcarbamoyl)propyl, 2-

(N,N-dipropylcarbamoyl)-1-methylethyl, 4-(N,N-dipropylcarbamoyl)butyl, 1-(N,N-dimethylcarbamoyl)methyl-1-methylethyl, 5-(N-pentyl-N-hexylcarbamoyl)pentyl, 3-(N-pentyl-N-hexyl)hexyl, (1-aziridinylcarbonyl)methyl, 2-(1-azetidinylcarbonyl)ethyl, 2-(piperidinocarbonyl)ethyl, 3-(1-pyrrolidinylcarbonyl)propyl, 2-(1-piperidinocarbonyl)-1-methylethyl, 4-(1-azetidinylcarbonyl)butyl, 1-(1-aziridinylcarbonyl)methyl-1-methylethyl, 3-(1-pyrrolidinylcarbonyl)pentyl, 6-(piperidinocarbonyl)hexyl, etc.]; and the like.

The preferred substituent of "unsaturated heterocyclic group" may be lower alkyl, lower alkyl having hydroxy and halogen, hydroxy(lower)alkyl, lower alkoxy(lower)alkyl, carboxy(lower)alkyl, lower alkoxycarbonyl(lower)alkyl, carbamoyl(lower)alkyl, N,N-di(lower)alkylcarbamoyl(lower)alkyl wherein two lower alkyl groups on nitrogen atom may bond to each other to form 3 to 6-membered ring, carboxy(lower)alkenyl, di(lower)alkylamino, halogen, lower alkoxy, oxo, carboxy, lower alkoxycarbonyl, lower alkanoyl, amino, cyano and hydroxy,

in which the more preferred one may be (C_1-C_4)alkyl, (C_1-C_4)alkyl having hydroxy and halogen, hydroxy(C_1-C_4)alkyl, (C_1-C_4)alkoxy(C_1-C_4)alkyl, carboxy(C_1-C_4)alkyl, (C_1-C_4)alkoxycarbonyl(C_1-C_4)alkyl, carbamoyl(C_1-C_4)alkyl, N,N-di(C_1-C_4)alkylcarbamoyl(C_1-C_4)alkyl, piperidinocarbonyl(C_1-C_4)alkyl, carboxy(C_2-C_4)alkenyl, di(C_1-C_4)alkylamino, halogen, (C_1-C_4)alkoxy, oxo, carboxy, (C_1-C_4)alkoxycarbonyl, (C_1-C_4)alkanoyl, amino, cyano and hydroxy,

and the most preferred one may be methyl, propyl, 2-hydroxy-3,3,3-trichloropropyl, 2-hydroxyethyl, 3-hydroxypropyl, 2-ethoxyethyl, 2-carboxyethyl, 3-carboxypropyl, 4-carboxybutyl, methoxycarbonylmethyl, 2-methoxycarbonylethyl, 3-ethoxycarbonylpropyl, 4-ethoxycarbonylbutyl, 2-carbamoylethyl, 2-(N,N-dimethylcarbamoyl)ethyl, 2-(piperidinocarbonyl)ethyl, 2-carboxyvinyl, dimethylamino, chloro, methoxy, oxo, carboxy, ethoxycarbonyl, methoxycarbonyl, acetyl, amino, cyano and hydroxy.

Suitable "heterocyclic compound having

- moiety in its ring" may include saturated or unsaturated, monocyclic or polycyclic heterocyclic compound containing at least one hetero atom such as nitrogen, oxygen, sulfur or the like, which has

- moiety in its ring, and suitable examples thereof may include:

saturated or unsaturated 3 to 8-membered (more preferably 5 to 7-membered) heteromonocyclic compound containing 1 to 4 nitrogen atom(s) which has

- moiety in its ring, for example, azepine having oxo (e.g. 2-oxo-2H-azepine, etc.), pyrrole having oxo (e.g. 5-oxopyrroline, etc.), pyrroline having oxo (e.g. 2-oxopyrrolidine, etc.), imidazole having oxo (e.g. 4-oxoimidazoline, etc.), pyrazole having oxo (e.g. 5-oxopyrazoline, etc.), pyridine having oxo (e.g. 4-oxo-1,4-dihydropyridine, etc.), dihydropyridine having oxo (e.g. 2-oxo-1,2,3,4-tetrahydropyridine, 4-oxo-1,2,3,4-tetrahydropyridine, etc.), tetrahydropyridine having oxo (e.g. 2-oxopiperidine, 4-oxopiperidine, etc.), pyrimidine having oxo (e.g. 2-oxo-1,2-dihydropyrimidine, etc.), dihydropyrimidine having oxo (e.g. 4-oxo-1,2,3,4-tetrahydropyrimidine, etc.), pyrazine having oxo (e.g. 2-oxo-1,2-dihydropyrazine, etc.), pyridazine having oxo (e.g. 3-oxo-3,4-dihydropyridazine, etc.), dihydropyridazine having oxo (e.g. 4-oxo-2,3,4,5-tetrahydropyridazine, 3-oxo-2,3,4,5-tetrahydropyridazine, etc.), dihydropyridazine having oxo (e.g. 3-oxo-perhydropyridazine, etc.), triazole having oxo (e.g. 3-oxo-2,3-dihydro-4H-1,2,4-triazole, 4-oxo-4,5-dihydro-1H-1,2,3-triazole, 5-oxo-1,5-dihydro-2H-1,2,3-triazole, etc.), tetrazole having oxo (e.g. 5-oxo-4,5-dihydro-1H-tetrazole, 5-oxo-1,5-dihydro-2H-tetrazole, etc.), etc.;

saturated or unsaturated condensed heterocyclic compound containing 1 to 4 nitrogen atom(s) which has

-moiety in its ring, for example, indole having oxo (e.g. 2-oxo-2,3-dihydroindole, etc.), isoindole having oxo (e.g. 7-oxo-6,7-dihydroisoindole, etc.), indolizine having oxo (e.g. 3-oxo-2,3-dihydroindolizine, etc.), benzimidazole having oxo (e.g. 2-oxo-2,3-dihydro-1H-benzimidazole, etc.), quinoline having oxo (e.g. 4-oxo-3,4-dihydroquinoline, etc.), dihydroquinoline having oxo (e.g. 5-oxo-1,4,5,6-tetrahydroquinoline, etc.), isoquinoline having oxo (e.g. 4-oxo-3,4-dihydroisoquinoline, etc.), indazole having oxo (e.g. 3-oxo-2,3-dihydro-1H-indazole, etc.), benzotriazole having oxo (e.g. 4-oxo-4,5-dihydro-1H-benzotriazole, etc.), etc.;

saturated or unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic compound containing 1 to 2 oxygen atom(s) and 1 to 3 nitrogen atom(s) which has

- moiety in its ring, for example, oxazole having oxo (e.g. 4-oxo-4,5-dihydroxazole, etc.), isoxazole having oxo (e.g. 3-oxo-2,3-dihydroisoxazole, etc.), dihydroisoxazole having oxo (e.g. 4-oxo-isoxazolidine, etc.), oxadiazole having oxo (e.g. 3-oxo-2,3-dihydro-1,2,4-oxadiazole, 3-oxo-2,3-dihydro-1,2,5-oxadiazole, etc.), etc.;

saturated or unsaturated condensed heterocyclic compound containing 1 to 2 oxygen atom(s) and 1 to 3

nitrogen atom(s) which has

- moiety in its ring, for example, benzoxazole having oxo (e.g. 2-oxo-2,3-dihydrobenzoxazole, etc.), benzoxadiazole having oxo (e.g. 5-oxo-4,5-dihydrobenzoxadiazole, etc.), etc.;

saturated or unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic compound containing 1 to 2 sulfur atom(s) and 1 to 3 nitrogen atom(s) which has

- moiety in its ring, for example, thiazole having oxo (e.g. 4-oxo-4,5-dihydrothiazole, etc.), dihydrothiazole having oxo (e.g. 4-oxo-thiazolidine, etc.), isothiazole having oxo (e.g. 3-oxo-2,3-dihydroisothiazole, etc.), thiadiazole having oxo (e.g. 4-oxo-4,5-dihydro-1,2,3-thiadiazole, 3-oxo-2,3-dihydro-1,2,4-thiadiazole, 2-oxo-2,3-dihydro-1,3,4-thiadiazole, 3-oxo-2,3-dihydro-1,2,5-thiadiazole, etc.), dihydrothiazine having oxo (e.g. 4-oxo-perhydro-1,3-thiazine, etc.), etc.;

saturated or unsaturated condensed heterocyclic compound containing 1 to 2 sulfur atom(s) and 1 to 3 nitrogen atom(s) which has

- moiety in its ring, for example, benzothiazole having oxo (e.g. 2-oxo-2,3-dihydrobenzothiazole, etc.), benzothiadiazole having oxo (e.g. 6-oxo-6,7-dihydrobenzothiadiazole, etc.), imidazothiadiazole having oxo (e.g. 5-oxo-5H-imidazo[2,1-b][1,3,4]thiadiazole, etc.), etc.;

saturated or unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic compound containing 1 to 2 sulfur atom(s) which has

- moiety in its ring, for example, thiophene having oxo (e.g. 3-oxo-2,3-dihydrothiophene, etc.), dihydrothiin having oxo (e.g. 5-oxo-thiane, etc.), etc.;

saturated or unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic compound containing an oxygen atom which has

- moiety in its ring, for example, furan having oxo (e.g. 3-oxo-2,3-dihydrofuran, etc.), dihydrofuran having oxo (e.g. 3-oxo-furrolane, etc.), etc.;

saturated or unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic compound containing an oxygen atom and 1 to 2 sulfur atom(s) which has

- moiety in its ring, for example, dihydroxathiin having oxo (e.g. 3-oxo-1,4-oxathiane, etc.), oxathiin having oxo (e.g. 3-oxo-2,3-dihydroxathiin, etc.), etc.;

saturated or unsaturated condensed heterocyclic compound containing 1 to 2 sulfur atom(s) which has

- moiety in its ring, for example, benzothiophene having oxo (e.g. 3-oxo-2,3-dihydrobenzo[b]thiophene, etc.), benzodithiin having oxo (e.g. 2-oxo-2,3-dihydrobenzo[b][1,4]dithiin, etc.), etc.;

saturated or unsaturated condensed heterocyclic compound containing an oxygen atom and 1 to 2 sulfur atom(s) which has

- moiety in its ring, for example, benzoxathiin having oxo (e.g. 6-oxo-5,6-dihydrobenz[b][1,4]oxathiin, etc.), etc.; and the like.

Aforesaid "heterocyclic compound having

- moiety in its ring" may have one or more (preferably 1 to 4) suitable substituent(s) as exemplified above for "suitable substituent(s)" of "unsaturated heterocyclic group".

Suitable "N-containing unsaturated heterocyclic compound having =N- moiety in its ring" may be heterocyclic compound containing at least one nitrogen atom and also containing at least one =N- moiety in its ring.

Suitable example of said "N-containing unsaturated heterocyclic compound having =N- moiety in its ring" may include :

unsaturated 3 to 8-membered (more preferably 5 to 7-membered) heteromonocyclic compound containing 1 to 4 nitrogen atom(s) having =N- moiety in its ring, for example, azepine (e.g. 1H-azepine, etc.) imidazole, pyrazole, pyridine, dihydropyridine (e.g. 3,4-dihydropyridine, 5,6-dihydropyridine, etc.), tetrahydropyridine (e.g. 3,4,5,6-tetrahydropyridine, etc.) pyrimidine, dihydropyrimidine (e.g. 1,2-dihydropyrimidine, etc.), pyrazine, pyridazine, dihydropyridazine (e.g. 2,3-dihydropyridazine, 1,4-dihydropyridazine, etc.), tetrahydropyridazine (e.g. 2,3,4,5-tetrahydropyridazine, etc.), triazole (e.g. 4H-1,2,4-triazole, 1H-1,2,3-triazole, 2H-1,2,3-triazole, etc.), tetrazole (e.g. 1H-tetrazole, 2H-tetrazole, etc.), etc.;

unsaturated condensed heterocyclic compound containing 1 to 4 nitrogen atom(s) having =N- moiety in its ring, for example, indole, benzimidazole, quinoline dihydroquinoline (e.g. 3,4-dihydroquinoline, etc.) isoquinoline, indazole, benzotriazole, etc.;

unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic compound containing 1 to 2 oxygen atom(s) and 1 to 3 nitrogen atom(s) having =N-moiety in its ring, for example, oxazole, isoxazole, dihydroisoxazole (e.g. 4,5-dihydroisoxazole, etc.) oxadiazole (e.g. 1,2,4-oxadiazole, 1,3,4-oxadiazole, 1,2,5-oxadiazole, etc.), etc.;

unsaturated condensed heterocyclic compound containing 1 to 2 oxygen atom(s) and 1 to 3 nitrogen atom(s), having =N- moiety in its ring, for example, benzoxazole, benzoxadiazole, etc.;

unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic compound containing 1 to 2 sulfur atom(s) and 1 to 3 nitrogen atom(s) having =N-moiety in its ring, for example, thiazole, dihydrothiazole (e.g. 4,5-dihydrothiazole, etc.) isothiazole, thiadiazole (e.g. 1,2,3-thiadiazole, 1,2,4-thiadiazole, 1,3,4-thiadiazole, 1,2,5-thiadiazole, etc.), dihydrothiazine, etc.;

unsaturated condensed heterocyclic compound containing 1 to 2 sulfur atom(s) and 1 to 3 nitrogen atom(s) having =N- moiety in its ring, for example, benzothiazole, benzothiadiazole, imidazothiadiazole, etc.

Aforesaid "N-containing unsaturated heterocyclic compound having =N- moiety in its ring" may have one or more (preferably 1 to 4) suitable substituent(s) as exemplified above for "suitable substituent(s)" of "unsaturated heterocyclic group".

Suitable "N-containing unsaturated heterocyclic group" may be unsaturated heterocyclic group containing at least one nitrogen atom as hetero atom and suitable examples thereof can be referred to unsaturated heterocyclic group containing at least one nitrogen atom as exemplified for "unsaturated heterocyclic group" before.

Aforesaid "N-containing unsaturated heterocyclic group" may have one or more (preferably 1 to 4) suitable substituent(s) as exemplified above for "suitable substituent(s)" of "unsaturated heterocyclic group".

Suitable "unsaturated heterocyclic group having cyano" may be "unsaturated heterocyclic group" as explained above which has cyano as its substituent, and said "unsaturated heterocyclic group having cyano" may have additionally one or more (preferably 1 to 4) suitable substituent(s) as exemplified above for "suitable substituent(s)" of "unsaturated heterocyclic group".

Suitable "unsaturated heterocyclic group having carboxy" may be "unsaturated heterocyclic group" as explained above which has carboxy as its substituent, and said "unsaturated heterocyclic group having carboxy" may have additionally one or more (preferably 1 to 4) suitable substituent(s) as exemplified above for "suitable substituent(s)" of "unsaturated heterocyclic group".

Suitable "unsaturated heterocyclic group having amino" may be "unsaturated heterocyclic group" as explained above which has amino as its substituent, and said "unsaturated heterocyclic group having amino" may have additionally one or more (preferably 1 to 4) suitable substituent(s) as exemplified above for "suitable substituent(s)" of "unsaturated heterocyclic group".

Suitable "unsaturated heterocyclic group having oxo" may be "unsaturated heterocyclic group" as explained above which has oxo as its substituent, and said "unsaturated heterocyclic group having oxo" may have additionally one or more (preferably 1 to 4) suitable substituent(s) as exemplified above for "suitable substituent(s)" of "unsaturated heterocyclic group".

Suitable "unsaturated heterocyclic group having halogen" may be "unsaturated heterocyclic group" as explained above which has halogen as its substituent, and said "unsaturated heterocyclic group having halogen" may have additionally one or more (preferably 1 to 4) suitable substituent(s) as exemplified above for "suitable substituent(s)" of "unsaturated heterocyclic group".

Suitable "unsaturated heterocyclic group having di(lower)alkylamino" may be "unsaturated heterocyclic group" as explained above which has di-lower)alkylamino as its substituent, and said "unsaturated heterocyclic group having di(lower)alkylamino" may have additionally one or more (preferably 1 to 4) suitable substituent(s) as exemplified above for "suitable substituent(s)" of "unsaturated heterocyclic group".

Suitable "unsaturated heterocyclic group having lower alkoxy" may be "unsaturated heterocyclic group" as explained above which has lower alkoxy as its substituent, and said "unsaturated heterocyclic group having lower alkoxy" may have additionally one or more (preferably 1 to 4) suitable substituent(s) as exemplified above for "suitable substituent(s)" of "unsaturated heterocyclic group".

Suitable "unsaturated heterocyclic group which may have one or more suitable substituent(s) except carboxy" may be "unsaturated heterocyclic group" as explained above which may have one or more (preferably 1 to 4) suitable substituent(s), as exemplified for "suitable substituent(s)" of "unsaturated heterocyclic group", except carboxy.

Suitable "unsaturated cyclic amino group" may include unsaturated, monocyclic or polycyclic amino group which may contain additional hetero atom such as nitrogen, oxygen, sulfur or the like.

Suitable examples of said "unsaturated cyclic amino group" may include :

unsaturated 3 to 8-membered (more preferably 5 to 7-membered) heteromonocyclic amino group containing 1 to 4 nitrogen atom(s), for example, azepin-1-yl (e.g. 1H-azepin-1-yl, etc.) 1-pyrrolyl, 1-pyrrolinyl, 1-imidazolyl, 1-pyrazolyl, dihydropyridin-1-yl (e.g. 1,2-dihydropyridin-1-yl, 1,4-dihydropyridin-1-yl, etc.), tetrahydropyridyl (e.g. 1,2,3,6-tetrahydropyridin-1-yl, etc.) dihydropyrimidinyl (e.g. 1,2-dihydropyrimidin-1-yl, etc.), dihydropyridazinyl (e.g. 2,3-dihydropyridazin-2-yl, 1,4-dihydropyridazin-1-yl, etc.), tetrahydropyridazinyl (e.g. 2,3,4,5-tetrahydropyridazin-2-yl, etc.) triazolyl (e.g. 4H-1,2,4-triazol-4-yl, 1H-1,2,3-triazol-1-yl, 2H-1,2,3-triazol-2-yl, etc.), tetrazol (e.g. 1H-tetrazol-1-yl, 2H-tetrazol-2-yl, etc.) etc.;

unsaturated condensed heterocyclic amino group containing 1 to 4 nitrogen atom(s), for example, 1-indolyl, 2-isoindolyl, benzimidazol-1-yl, dihydroquinolyl (e.g. 1,2-dihydroquinolin-1-yl, etc.) indazolyl (e.g. 1H-indazol-1-yl, etc.), benzotriazolyl (e.g. 1H-benzotriazol-1-yl, etc.), etc.;

unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic amino group containing 1 to 2 oxygen atom(s) and 1 to 3 nitrogen atom(s), for example dihydroxazolyl (e.g. 2,3-dihydroxazol-3-yl, etc.) dihydroisoxazolyl (e.g. 2,5-dihydroisoxazol-2-yl, etc.), etc.;

unsaturated condensed heterocyclic amino group containing 1 to 2 oxygen atom(s) and 1 to 3 nitrogen atom(s), for example, 2,3-dihydrobenzoxazol-3-yl, 2,3-dihydrobenz[d][1,2,3]oxadiazol-2-yl, etc.;

unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic amino group containing 1 to 2 sulfur atom(s) and 1 to 3 nitrogen atom(s), for example, dihydrothiazolyl (e.g. 2,3-dihydrothiazol-3-yl, etc.) dihydrothiadiazolyl (e.g. 2,3-dihydro-1,2,3-thiadiazol-2-yl,
4,5-dihydro-1,2,4-thiadiazol-4-yl,
3,4-dihydro-1,3,4-thiadiazol-3-yl,
2,3-dihydro-1,2,5-thiadiazol-2-yl, etc.), dihydrothiazinyl (e.g. 2,3-dihydro-4H-1,4-thiazin-4-yl, etc.), etc.;

unsaturated condensed heterocyclic amino group containing 1 to 2 sulfur atom(s) and 1 to 3 nitrogen atom(s), for example, dihydrobenzothiazolyl (e.g. 2,3-dihydrobenzothiazol-3-yl, etc.), tetrahydrobenzothiadiazolyl (e.g. 2,3,4,5-tetrahydrobenzo[d][1,2,3]thiadiazol-2-yl, etc.), dihydroimidazothiadiazolyl (e.g. 3,4-dihydro-2H-imidazo[2,1-b][1,3,4]thiadiazol-3-yl, etc.), etc.;

in which the preferred one may be unsaturated 3 to 8-membered heteromonocyclic amino group containing 1 to 4 nitrogen atom(s) and unsaturated condensed heterocyclic amino group containing 1 to 2 sulfur atom(s) and 1 to 3 nitrogen atom(s), the more preferred one may be dihydropyridazinyl, tetrahydropyridazinyl, dihydropyrimidinyl, dihydropyridyl, tetrahydropyridyl and pyrazolyl, and the most preferred one may be 2,3-dihydropyridazin-2-yl, 1,4-dihydropyridazin-1-yl, 2,3,4,5-tetrahydropyridazin-2-yl, 1,2-dihydropyrimidin-1-yl, 1,2-dihydropyridin-1-yl, 1,4-dihydropyridin-1-yl, 1,2,3,6-tetrahydropyridin-1-yl, and pyrazol-1-yl.

Aforesaid "unsaturated cyclic amino group" may have one or more (preferably 1 to 4) suitable substituent(s) as exemplified above for "suitable substituent(s) of "unsaturated heterocyclic group".

Suitable "a leaving group" may include di(lower)alkylamino (e.g. dimethylamino, diethylamino, N-ethylpropylamino, dibutylamino, N-pentylhexylamino, etc.), lower alkoxy as mentioned above, halogen as mentioned above, lower alkylthio (e.g. methylthio, ethylthio, propylthio, butylthio, pentylthio, hexylthio, etc.), acyloxy such as lower alkanoyloxy (e.g. acetoxy, etc.), sulfonyloxy (e.g. mesyloxy, tosyloxy, etc.) or the like, and the like.

The processes for preparing the object compound (I) of the present invention are explained in detail in the following.

Process 1

The object compound (I) or a salt thereof can be prepared by reacting the compound (II) or a salt thereof with the compound (III) or a salt thereof.

Suitable salt of the compound (II) can be referred to acid addition salt as exemplified for the compound (I).

Suitable salt of the compound (III) can be referred to the ones as exemplified for the compound (I).

This reaction is preferably carried out in a solvent such as acetic acid, benzene, pyridine or any other solvent which does not adversely affect the reaction.

This reaction may be carried out in the presence of an acid such as sulfuric acid, hydrochloric acid, p-toluenesulfonic acid or the like.

The reaction temperature is not critical and the reaction is usually carried out under warming to heating.

Process 2

The object compound (Ia) or a salt thereof can be prepared by reacting the compound (II) or a salt thereof with the compound (IV) or a salt thereof.

Suitable salt of the compound (Ia) can be referred to the ones as exemplified for the compound (I).

Suitable salt of the compound (II) can be referred to an acid addition salt as exemplified for the compound (I).

Suitable salt of the compound (IV) can be referred to the ones as exemplified for the compound (I).

In this reaction, the group R^3 i.e. an acyl group) may be introduced into the compound (IV) during this reaction by carrying out this reaction in the presence of an acylating agent such as lower alkyl haloformate (e.g. methyl chloroformate, ethyl chloroformate, etc.), acid halide (e.g. acetyl chloride, propionyl bromide, etc.).

This reaction is usually carried out in a solvent such as methylene chloride, chloroform, tetrahydrofuran, N,N-dimethylformamide or any other solvent which does not adversely influence the reaction.

The reaction temperature is not critical and the reaction is usually carried out at room temperature, under warming to heating.

There is a case where the group R^3 is removed during the reaction, isolation step or purification step, and this case is also included within the scope of the present invention.

Process 3

The object compound (Ib) or a salt thereof can be prepared by subjecting the compound (Ia) or a salt thereof to removal reaction of an acyl group.

Suitable salt of the compound (Ib) can be referred to the ones as exemplified for the compound (I).

The removal reaction of this process can be carried out in the dehydrogenation condition (e.g. potassium t-butoxide in t-butanol, manganese oxide in chloroform , etc.), conventional hydrolysis condition [e.g. alkali metal hydroxide (e.g. sodium hydroxide, potassium hydroxide, etc.) in alcohol (e.g. methanol, ethanol, etc.) and water; or the like.

The reaction condition can be selected according to the kind of the compound (Ia) to be used.

The reaction temperature is not critical and the reaction is usually carried out at room temperature, under warming to heating.

Process 4

The object compound (Id) or a salt thereof can be prepared by subjecting the compound (Ic) or a salt thereof to introduction reaction of lower alkyl which may have one or more suitable substituent(s).

Suitable salt of the compound (Id) can be referred to the ones as exemplified for the compound (I).

The introduction reaction of this process can be carried out by reacting the compound (Ic) or a salt thereof with a reagent for introduction of lower alkyl which may have one or more suitable substituent(s).

Suitable reagent for introduction of lower alkyl which may have one or more suitable substituent(s) can include a compound of the formula :

$R^4 - X$

[wherein R^4 is as defined above and X is a leaving group such as an acyloxy [e.g. lower alkanoyloxy (e.g. formyloxy, acetoxy, propionyloxy, butyryloxy, pivaloyloxy, hexanoyloxy, etc.), sulfonyloxy (e.g. mesyloxy, tosyloxy, etc.), etc.], halogen (e.g. fluoro, chloro, bromo, iodo) or the like]; acyl(lower)alkene in which the double bond is adjacent to acyl group such as acrylic acid and its derivative (e.g. methyl acrylate, ethyl acrylate, etc.), crotonic acid and its derivative (e.g. methyl crotonate, ethyl crotonate, etc.); and the like.

This reaction is usually carried out in a solvent such as diethyl ether, chloroform, methylene chloride, N,N-dimethylformamide, alcohol (e.g. methanol, ethanol, etc.) or any other solvent which does not adversely influence the reaction.

The reaction temperature is not critical and the reaction is usually carried out under cooling, at room temperature, under warming to heating.

The reaction can be carried out in the presence of condensation catalyst (e.g. trimethylbenzylammonium hydroxide, etc.).

Process 5

The object compound (If) or a salt thereof can be prepared by subjecting the compound (Ie) or a salt thereof to removal reaction of carboxy protective group.

Suitable salts of the compounds (Ie) and (If) can be referred to the ones as exemplified for the compound (I).

This reaction is carried out in accordance with a conventional method such as hydrolysis or the like.

The hydrolysis is preferably carried out in the presence of a base or an acid including Lewis acid.

Suitable base may include an inorganic base and an organic base such as an alkali metal [e.g. sodium, potassium, etc.], an alkaline earth metal [e.g. magnesium, calcium, etc.], the hydroxide or carbonate or bicarbonate thereof, trialkylamine [e.g. trimethylamine, triethylamine, etc.],picoline, 1,5-diazabicyclo[4.3.0]-non-5-ene, 1,4-diazabicyclo[2.2.2]octane, 1,8-diazabicyclo[5.4.0]undec-7-ene, or the like.

Suitable acid may include an organic acid [e.g. formic acid, acetic acid, propionic acid, trichloroacetic acid, trifluoroacetic acid, etc.] and an inorganic acid [e.g. hydrochloric acid, hydrobromic acid, sulfuric acid, hydrogen chloride, hydrogen bromide, etc.].

The elimination using Lewis acid such as trihaloacetic acid [e.g. trichloroacetic acid, trifluoroacetic acid, etc.] or the like is preferably carried out in the presence of cation trapping agents [e.g. anisole, phenol, etc.].

The reaction is usually carried out in a solvent such as water, an alcohol [e.g. methanol, ethanol, etc.], methylene chloride, tetrahydrofuran, a mixture thereof or any other solvent which does not adversely influence the reaction. A liquid base or acid can be also used as the solvent.

The reaction temperature is not critical and the reaction is usually carried out under cooling to warming.

Process 6

The object compound (Ig) or a salt thereof can be prepared by subjecting the compound (V) or a salt thereof to formation reaction of pyridazinone ring.

Suitable salts of the compounds (Ig) and (V) can be referred to acid addition salts as exemplified for the compound (I).

The formation reaction of this process can be carried out, for example, by reacting the compound (V) or a salt thereof with glyoxalic acid or its reactive derivative or a salt thereof and hydrazine or a salt thereof.

Suitable salt of glyoxalic acid can be referred to a salt with a base as exemplified for the compound (I).

Suitable salt of hydrazine can be referred to an acid addition salt as exemplified for the compound (I).

Suitable reactive derivative of glyoxalic acid may be the ones conventionally used in this field of the art such as an activated ester thereof.

The reaction can be carried out in the presence or absence of a solvent.

The reaction temperature is not critical and the reaction is usually carried out under warming to heating.

Process 7

The object compound (Ih) or a salt thereof can be prepared by reacting the compound (VI) or a salt thereof with the compound (VII) or a salt thereof.

Suitable salts of the compounds (Ih), (VI) and (VII) can be referred to acid addition salt as exemplified for the compound (I).

This reaction can be carried out, for example, according to the procedure as disclosed in Example 15.

Process 8

The object compound (Ii) or a salt thereof can be prepared by reacting the compound (VIII) or a salt thereof with the compound (IX) or its reactive derivative at methyl group or a salt thereof.

Suitable salts of the compounds (Ii), (VIII) and (IX) can be referred to acid addition salt as exemplified for the compound (I).

This reaction can be carried out, for example, according to the procedure as disclosed in Example 16.

Suitable reactive derivative at methyl group of the compound (IX) may be its pyridinium derivative or the like.

Process 9

The object compound (Ij) or a salt thereof can be prepared by reacting the compound (X) or a salt thereof with the compound (XI) or a salt thereof.

Suitable salt of the compound (Ij), (X) and (XI) can be referred to acid addition salt as exemplified for the compound (I).

This reaction can be carried out, for example, according to the procedure as disclosed in Example 17.

Process 10

The object compound (Ik) or a salt thereof can be prepared by reacting the compound (XII) or a salt thereof with the compound (XI) or a salt thereof.

Suitable salt of the compound (Ik), (XII) and (XI) can be referred to acid addition salt as exemplified for the compound (I).

This reaction can be carried out, for example, according to the procedure as disclosed in Example 18.

Process 11

The object compound (Il) or a salt thereof can be prepared by reacting the compound (XIII) or a salt thereof with the compound (XIV) or a salt thereof.

Suitable salt of the compounds (Il), (XIII) and (XIV) can be referred to acid addition salt as exemplified for the compound (I).

This reaction can be carried out, for example, according to the procedure as disclosed in Example 19.

Process 12

The object compound (Im) or a salt thereof can be prepared by reacting the compound (XV) or a salt thereof with the compound (XVI) or a salt thereof.

Suitable salt of the compounds (Im), (XV) and (XVI) can be referred to acid addition salt as exemplified for the compound (I).

This reaction can be carried out, for example, according to the procedure as disclosed in Example 20.

Process 13

The object compound (In) or a salt thereof can be prepared by reacting the compound (XV) or a salt thereof with the compound (XVII) or a salt thereof.

Suitable salt of the compounds (In), (XV) and (XVII) can be referred to acid addition salt as exemplified for the compound (I).

This reaction can be carried out, for example, according to the procedure as disclosed in Example 21.

Process 14

The object compound (Io) or a salt thereof can be prepared by reacting the compound (XV) or a salt thereof with the compound (XVIII) or a salt thereof.

Suitable salt of the compounds (Io), (XV) and (XVIII) can be referred to acid addition salt as exemplified for the compound (I).

This reaction can be carried out, for example, according to the procedure as disclosed in Example 23.

Process 15

The object compound (Iq) or a salt thereof can be prepared by subjecting the compound (Ip) or a salt thereof to hydrolysis reaction of cyano group.

Suitable salts of the compounds (Ip) and (Iq) can be referred to the ones as exemplified for the compound (I).

This hydrolysis reaction can be carried out according to a similar manner to that disclosed in the explanation of Process 5.

Process 16

The object compound (Ir) or a salt thereof can be prepared by subjecting the compound (Iq) or a salt thereof to removal reaction of carboxy group.

Suitable salts of the compounds (Iq) and (Ir) can be referred to the ones as exemplified for the compound (I).

This reaction can be carried out, for example, according to the procedure as disclosed in Example 45.

Process 17

The object compound (Is) or a salt thereof can be prepared by subjecting the compound (If) or a salt thereof to amidation reaction.

Suitable salts of the compounds (If) and (Is) can be referred to the ones as exemplified for the compound (I).

This reaction can be carried out by reacting the compound (If) or a salt thereof with an amidation reagent such as ammonia, di(lower)alkylamine wherein two lower alkyl groups may bond to each other to form 3 to 6-membered ring (e.g. dimethylamine, N-methylethylamine, diethylamine, dipropylamine, N-butyl-t-butylamine, dipentylamine, N-pentylhexylamine, aziridine, azetidine, pyrrolidine, piperidine, etc.) or the like.

The reaction is usually carried out in a conventional solvent such as water, alcohol [e.g. methanol, ethanol, etc.], acetone, dioxane, acetonitrile, chloroform, methylene chloride, ethylene chloride, tetrahydrofuran, ethyl acetate, N,N-dimethylformamide, pyridine or any other organic solvent which does not adversely influence the reaction. These conventional solvent may also be used in a mixture with water.

In this reaction, when the compound (If) is used in a free acid form or its salt form, the reaction is preferably carried out in the presence of a conventional condensing agent such as N,N'-dicyclohexylcarbodiimide; or the like.

The reaction may also be carried out in the presence of an inorganic or organic base such as an alkali metal carbonate, alkali metal bicarbonate, tri(lower)alkylamine (e.g. triethylamine, etc.), pyridine N-(lower)-alkylmorpholine, N,N-di-lower)alkylbenzylamine, or the like.

The reaction temperature is not critical, and the reaction is usually carried out under cooling to warming.

Process 18

The object compound (Iu) or a salt thereof can be prepared by subjecting the compound (It) or a salt thereof to conversion reaction of amino group to oxo group.

Suitable salts of the compounds (It) and (Iu) can be referred to the ones as exemplified for the compound (I).

This reaction can be carried out, for example, according to the procedure as disclosed in Example 52.

Process 19

The object compound (Iv) or a salt thereof can be prepared by subjecting the compound (Iu) or a salt thereof to removal reaction of carboxy group.

Suitable salt of the compounds (Iu) and (Iv) can be referred to the ones as exemplified for the compound (I).

This reaction can be carried out, for example, according to the procedure as disclosed in Example 54.

Process 20

The object compound (Iw) or a salt thereof can be prepared by reacting the compound (Iv) or a salt thereof with the compound (XIX) or a salt thereof.

Suitable salts of the compounds (Iv) and (Iw) can be referred to the ones as exemplified for the compound (I).

Suitable salt of the compound (XIX) can be referred to acid addition salt as exemplified for the compound (I).

This reaction can be carried out, for example, according to the procedure as disclosed in Example 57.

Process 21

The object compound (Ix) or a salt thereof can be prepared by subjecting the compound (Iv) or a salt thereof to conversion reaction of halogen to lower alkoxy.

Suitable salt of the compounds (Iv) and (Ix) can be referred to the ones as exemplified for the compound (I).

This reaction can be carried out, for example, according to the procedure as disclosed in Example 58.

Process 22

The object compound (Iu) or a salt thereof can be prepared by subjecting the compound (Ix) or a salt thereof to conversion reaction of lower alkoxy to oxo group.

Suitable salt of the compounds (Iu) and (Ix) can be referred to the ones as exemplified for the compound (I).

This reaction can be carried out, for example, according to the procedure as disclosed in Example 62.

Process 23

The object compound (Iy) or a salt thereof can be prepared by reacting the compound (XX) or a salt thereof with the compound (XXI) and ammonia.

Suitable salts of the compounds (Iy) and (XX) can be referred to acid addition salt as exemplified for the compound (I).

This reaction can be carried out, for example, according to the procedure as disclosed in Example 99.

The object compound (I) and a salt thereof possess various actions as stated above and useful as stated before.

The object compound (I) and a salt thereof have high solubility into water and are advantageous in preparing a pharmaceutical preparation.

In order to illustrate the usefulness of the object compound (I), the test results on diuretic activity of the representative compounds of the present invention are shown in the following.

Test on Diuretic Activity (1)

1. Test compound

3-[2-(2-Carboxyethyl)-3-oxo-2,3-dihydropyridazin-6-yl]-2-phenylpyrazolo[1,5-a]pyridine

2. Test Method

Male JCL:SD strain rats aged 6 weeks and weighing about 200 g were used after starving for 18 hours. Immediately after oral dosing with the test compound suspended in 0.5% methylcellulose (0.5% MC), the animals were given 20 ml/kg physiological saline orally. The rats were housed by threes in a metabolism

cage. The urine was collected for 3 hours. Urinary electrolyte (Na^+) was measured with a Stat/Ion^R System (Technichon). The tests were conducted in 3 groups of 3 animals each.

3. Test Result

The urinary electrolyte (Na^+) (%, control = 100%) was shown in the following table.

Dose (mg/kg)	Na^+
10.0	244

Test on Diuretic Activity (2)

1. Test Compound

Sodium salt of 3-[2-(3-carboxypropyl)-3-oxo-2,3-dihydropyridazin-6-yl]-2-phenylpyrazolo[1,5-a]pyridine

2. Test Method

Male JCL:SD strain rats aged 6 weeks and weighing about 200 g were used after starving for 18 hours. Immediately after oral dosing with the test compound suspended in 0.5% methylcellulose (0.5% MC), the animals were given 20 ml/kg physiological saline orally. The rats were housed by threes in a metabolism cage. The urine was collected for 6 hours. Urinary electrolyte (Na^+) was measured with a Stat/Ion^R System (Technichon). The tests were conducted in 3 groups of 3 animals each.

3. Test Result

ED_{100} value (mg/kg) was as follows.

ED_{100} = 0.31

For therapeutic administration, the object compound (I) and a pharmaceutically acceptable salt thereof of the present invention are used in the form of conventional pharmaceutical preparation which contains said compound as an active ingredient, in admixture with pharmaceutically acceptable carriers such as an organic or inorganic solid or liquid excipient which is suitable for oral, parenteral and external administration.

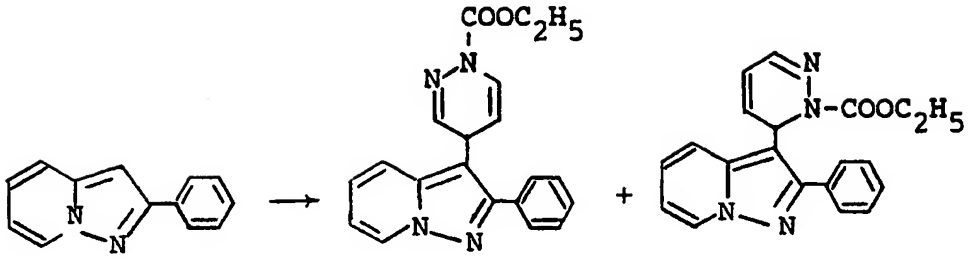
The pharmaceutical preparations may be in solid form such as tablet, granule, powder, capsule, or liquid form such as solution, suspension, syrup, emulsion, lemonade and the like.

If needed, there may be included in the above preparations auxiliary substances, stabilizing agents, wetting agents and other commonly used additives such as lactose, citric acid, tartaric acid, stearic acid, magnesium stearate, terra alba, sucrose, corn starch, talc, gelatin, agar, pectin, peanut oil, olive oil, cacao butter, ethylene glycol, and the like.

While the dosage of the compound (I) may vary from and also depend upon the age, conditions of the patient, a kind of diseases, a kind of the compound (I) to be applied, etc. In general, amounts between 1 mg and about 1,000 mg or even more per day may be administered to a patient. An average single dose of about 1 mg, 5 mg, 10 mg, 20 mg of the object compound (I) of the present invention may be used as diuretic and antihypertensive agent.

The following Examples are given for the purpose of illustrating the present invention in more detail.

Example 1



compound (A) compound (B)

Ethyl chloroformate (3.38 g) was added dropwise with stirring to a solution of 2-phenylpyrazolo[1,5-a]-pyridine (2.54 g) and pyridazine (5.00 g) in methylene chloride (5.0 ml) at 10 °C. After being stirred at 10 °C for 1 hour and then at room temperature for 2 hours, the reaction mixture was poured onto ice-water (100 ml) and extracted with ethyl acetate. The combined extracts were washed with saturated sodium chloride aqueous solution (100 ml), dried over magnesium sulfate and evaporated in vacuo. The residue was chromatographed on silica gel (150 g) with a mixture of chloroform and n-hexane (1:1) as an eluant. The fractions containing main-product [compound (A)] were combined and evaporated in vacuo to give 3-(1-ethoxycarbonyl-1,4-dihydropyridazin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine (2.42 g).

mp : 173-174 °C

IR (Nujol) : 1740, 1700, 1670, 1635, 1615 cm^{-1}

NMR ($CDCl_3$, δ) : 1.40 (3H, t, J=7.0Hz), 4.43 (2H, q, J=7.0Hz), 4.48-4.70 (1H, m), 5.03 (1H, dt, J=8.5Hz and 3.0Hz), 6.67-7.82 (10H, m), 8.50 (1H, dd, J=7.0Hz and 1.0Hz)

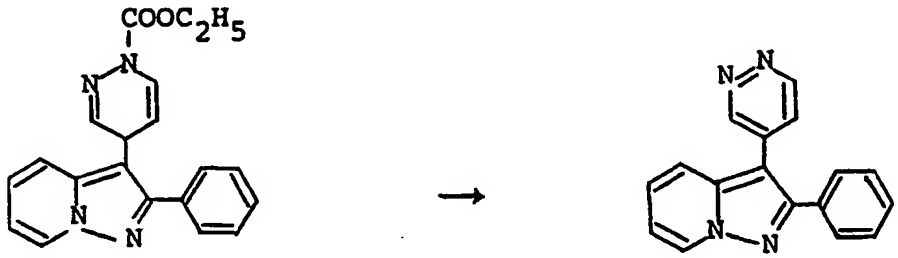
The fractions containing by-product [compound (B)] were combined and evaporated in vacuo to give 3-(2-ethoxycarbonyl-2,3-dihydropyridazin-3-yl)-2-phenylpyrazolo[1,5-a]pyridine (0.39 g).

mp : 150-152 °C

IR (Nujol) : 1720, 1635 cm^{-1}

NMR ($CDCl_3$, δ) : 1.16 (3H, t, J=7.0Hz), 4.18 (2H, q, J=7.0Hz), 5.67-7.95 (12H, m), 8.48 (1H, dd, J=7.0Hz and 1.0Hz)

Example 2



Air was bubbled into a mixture of 3-(1-ethoxycarbonyl-1,4-dihydropyridazin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine (1.12 g) and potassium tert-butoxide (1.81 g) in tert-butanol (25 ml) at 50 °C for 10 minutes.

tert-Butanol was evaporated in vacuo and ice-water (50 ml) was added to the residue. The mixture was extracted with chloroform (30 ml, 3 times). The combined extracts were washed with saturated sodium chloride aqueous solution (50 ml), dried over magnesium sulfate and evaporated in vacuo. The residue was chromatographed on silica gel (20 g) with chloroform as an eluant. The fractions containing the object compound were combined and evaporated in vacuo to give 3-(pyridazin-4-yl)-2-phenylpyrazolo[1,5-a]-pyridine (0.35 g).

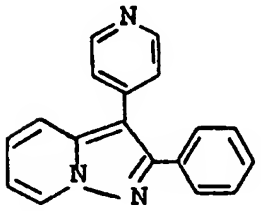
mp : 204-205 °C

IR (Nujol) : 1630, 1580, 1515 cm^{-1}

NMR (DMSO-d_6, δ) : 6.97-8.00 (9H, m), 8.85 (1H, d, J=7.0Hz), 9.03-9.27 (2H, m)

Analysis Calcd. for $C_{17}H_{12}N_4$	
Found :	C 74.98, H 4.44, N 20.58 C 75.27, H 4.63, N 20.38

Example 3



3-(Pyridin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine was prepared according to the similar manners to those of Example 1 and 2.
mp : 166-167°C
IR (Nujol) : 1630, 1600, 1530 cm^{-1}
NMR ($CDCl_3$, δ) : 6.83 (1H, dt, J = 1.5Hz and 7.0Hz), 7.20-7.83 (9H, m), 8.45-8.83 (3H, m)

Analysis Calcd. for $C_{18}H_{13}N_3$	
Found :	C 79.68, H 4.83, N 15.49 C 80.20, H 4.86, N 15.56

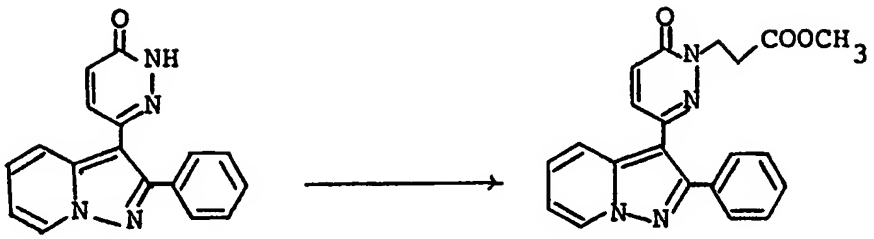
Example 4

A mixture of 3-acetyl-2-phenylpyrazolo[1,5-a]pyridine (40.00 g) and glyoxalic acid monohydrate (20.27 g) were stirred and heated at 100°C for 2.5 hours. The reaction mixture was dissolved in a mixture of ethyl acetate (220 ml) and aqueous sodium hydroxide (12%; 220ml). The aqueous layer was washed with 100 ml of chloroform, then acidified by 10% aqueous hydrochloric acid. That was extracted with chloroform (150 ml x 2). The extracts were combined, washed with saturated aqueous solution of sodium chloride. The solvent was evaporated and the residue (39.8 g) was dissolved in aqueous solution of ammonia (120 ml) and to the solution hydrazine monohydrate (42 g) was added. That mixture was refluxed for 2 hours. The precipitates were collected by filtration to give 3-(3-oxo-2,3-dihydropyridazin-6-yl)-2-phenylpyrazolo[1,5-a]pyridine (14.45 g).

mp : 212-214°C
IR (Nujol) : 1660, 1625, 1580, 1510 cm^{-1}
NMR ($CDCl_3$, δ) : 6.87 (1H, d, J=11Hz), 7.00 (1H, td, J=7Hz and 1Hz), 7.08 (1H, d, J=11Hz), 7.23-7.73 (6H, m), 7.83 (1H, d, J=8Hz), 7.77 (1H, d, J=7Hz)

Analysis Calcd. for $C_{17}H_{12}N_4O$	
Found :	C 70.82, H 4.20, N 19.43 C 70.75, H 4.83, N 19.24

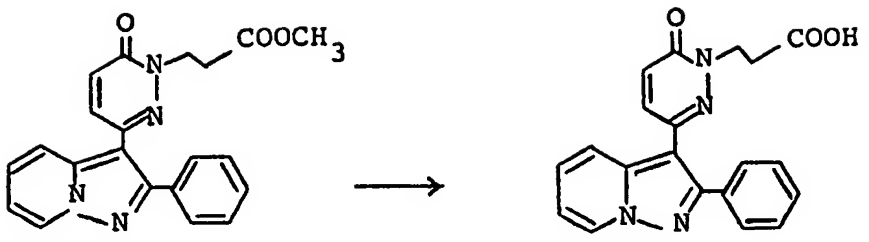
Example 5



A mixture of 3-(3-oxo-2,3-dihydropyridazin-6-yl)-2-phenylpyrazolo[1,5-a]pyridine (0.43 g), methyl acrylate (1.29 g), 40% methanolic trimethylbenzylammonium hydroxide (0.4 ml) and methanol (2 ml) in chloroform (8 ml) was refluxed for 40 minutes and then evaporated in vacuo. To the residue were added methylene chloride (30 ml) and water (30 ml), and the organic layer was separated, dried over magnesium sulfate and evaporated in vacuo. The crystalline residue was recrystallized from a mixture of ethyl acetate and diethyl ether to give 3-[2-(2-methoxycarbonylethyl)-3-oxo-2,3-dihydropyridazin-6-yl]-2-phenylpyrazolo-[1,5-a]pyridine (0.37 g).
mp : 133 to 133.5°C
IR (Nujol) : 1730, 1660, 1585 cm^{-1}
NMR ($CDCl_3$, δ) : 2.90 (2H, t, J=6Hz), 3.67 (3H, s), 4.57 (2H, t, J=6Hz), 6.70 (1H, d, J=9Hz), 6.87 (1H, t, J=7Hz), 7.00 (1H, d, J=9Hz), 7.17-7.73 (6H, m), 8.00 (1H, d, J=9Hz), 8.50 (1H, d, J=7Hz)
MS (M^+) : 374

Analysis Calcd. for $C_{21}H_{18}N_4O_2$	
Found :	C 67.37, H 4.85, N 14.96 C 67.31, H 5.35, N 14.94

Example 6



A mixture of 3-[2-(2-methoxycarbonylethyl)-3-oxo-2,3-dihydropyridazin-6-yl]-2-phenylpyrazolo[1,5-a]-pyridine (1.94 g) and 24% aqueous sodium hydroxide (2 ml) in methanol (8 ml) was refluxed for 30 minutes and then evaporated in vacuo. The residue was dissolved in water (30 ml) and the aqueous solution was acidified with hydrochloric acid, and extracted with chloroform (25 ml). The extract was dried over magnesium sulfate and evaporated in vacuo. The residue was recrystallized from a mixture of ethanol and n-hexane to give 3-[2-(2-carboxyethyl)-3-oxo-2,3-dihydropyridazin-6-yl]-2-phenylpyrazolo[1,5-a]pyridine (1.24 g).

mp : 155.5 to 156° C

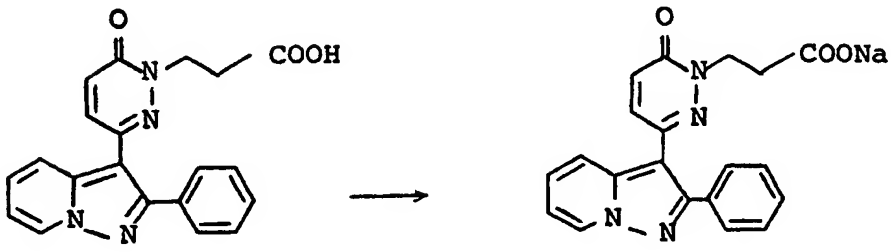
IR (Nujol) : 1835, 1640, 1570, 1520, 1490 cm^{-1}

NMR ($CDCl_3$, δ) : 2.97 (2H, t, J = 7Hz), 4.60 (2H, t, J = 7Hz), 6.15-7.00 (1H, broad d), 6.75-7.70 (9H, m), 8.00 (1H, d, J = 9Hz), 8.53 (1H, d, J = 7Hz)

MS (M^+) : 360

Analysis Calcd. for $C_{20}H_{16}N_4O_3$	
Found :	C 66.66, H 4.47, N 15.55 C 66.61, H 4.61, N 15.50

Example 7



To a mixture of 3-[2-(2-carboxyethyl)-3-oxo-2,3-dihydropyridazin-6-yl]-2-phenylpyrazolo[1,5-a]pyridine (10.0 g), ethanol (100 ml) and water (10 ml) was added a solution of sodium hydroxide (1.11 g) in a mixture of ethanol (40 ml) and water (15 ml). The reaction mixture was refluxed for 2 hours to give a clear solution, then this solution was cooled. The resultant solid was collected by filtration and washed with 85% ethanol (8 ml) and recrystallized twice from 83% ethanol (48 ml) to give crystals of sodium salt of 3-[2-(2-carboxyethyl)-3-oxo-2,3-dihydropyridazin-6-yl]-2-phenylpyrazolo[1,5-a]pyridine (5.13 g).

mp : 271-272° C

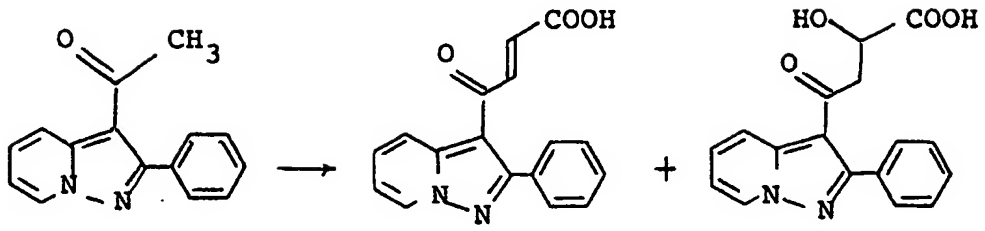
IR (Nujol) : 3400, 1670, 1610, 1580, 1530 cm^{-1}

NMR (DMSO-d_6, δ) : 2.45 (2H, t, J = 8Hz), 4.29 (2H, t, J = 8Hz), 6.81 (1H, d, J = 9Hz), 7.02 (1H, d, J = 9Hz), 7.07 (1H, td, J = 7Hz and 1Hz), 7.40-7.63 (6H, m), 8.02 (1H, d, J = 9Hz), 8.80 (1H, d, J = 7Hz)

MS : 360 (M^+)

Analysis Calcd. for $C_{20}H_{15}N_4O_3Na \cdot 3/2H_2O$ (%)	
Found :	C 58.67, H 4.43, N 13.69 C 58.49, H 4.27, N 13.96

Preparation 1



A mixture of glyoxylic acid monohydrate (3.50 g) and 3-acetyl-2-phenylpyrazolo[1,5-a]pyridine (5.00 g) was stirred and heated at 100°C for 4 hours. The warm reaction mixture was dissolved in methylene chloride (50 ml), and then extracted with 1N aqueous solution of sodium hydroxide (50 ml). The aqueous layer was washed with methylene chloride (total 200 ml) and then with ethyl acetate (total 200 ml). The aqueous solution was adjusted to pH 4~5 with 10% hydrochloric acid. The isolated oil was extracted with chloroform. The extract was evaporated in vacuo and crystallized from methylene chloride to give 4-oxo-4-(2-phenylpyrazolo[1,5-a]pyridin-3-yl)crotonic acid (0.46 g).

mp : 205-206°C

IR (Nujol) : 1690, 1650, 1630, 1500 cm^{-1}

NMR (DMSO-d_6, δ) : 2.77-3.63 (1H, broad), 6.33 (1H, d, J=16Hz), 6.87 (1H, d, J=16Hz), 7.15 (1H, td, J=7Hz and 1Hz), 7.27-7.73 (6H, m), 8.18 (1H, d, J=9Hz), 8.80 (1H, d, J=7Hz)

MS : 292

The aqueous layer of the last extract was acidified to pH 1 and extracted with a mixture of chloroform and methanol (10:1). The organic layer was evaporated in vacuo. The residue was purified by silica gel column chromatography using a mixture of methanol and chloroform as an eluent to give 4-oxo-4-(2-phenylpyrazolo[1,5-a]pyridin-3-yl)-2-hydroxybutyric acid (0.06 g).

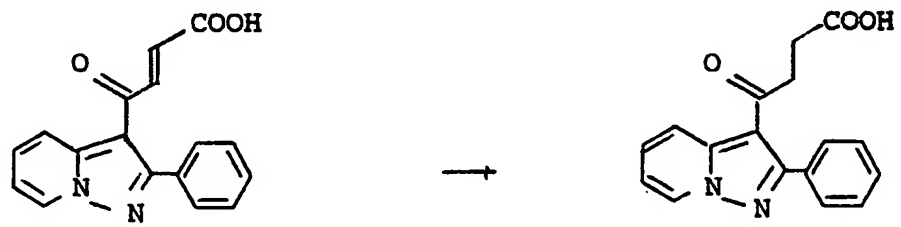
mp : 225°C (decomp)

IR (Nujol) : 3350, 1635, 1600, 1495 cm^{-1}

NMR (DMSO-d_6, δ) : 2.53-3.06 (3H, m), 4.06-4.30 (2H, m), 7.03 (1H, t, J=7Hz), 7.20-7.70 (6H, m), 8.13 (1H, d, J=9Hz), 8.70 (1H, d, J=7Hz)

MS : 292 (M-18)

Preparation 2



A mixture of 4-oxo-4-(2-phenylpyrazolo[1,5-a]pyridin-3-yl)crotonic acid (3.61 g), zinc powder (5.0 g) and

acetic acid (50 ml) was heated at 100° C for 1.5 hours. The zinc powder was filtered off and washed with acetic acid. The filtrate and washings were combined and evaporated in vacuo. To the residue a saturated aqueous solution of sodium hydrogen carbonate (50 ml) was added and extracted with ethyl acetate (50 ml x 2). The combined extracts were washed with a saturated aqueous solution of sodium chloride (50 ml), dried over magnesium sulfate and evaporated in vacuo. The residue was recrystallized from ethanol to give crystals of 4-oxo-4-(2-phenylpyrazolo[1,5-a]pyridin-3-yl)butyric acid (1.65 g).

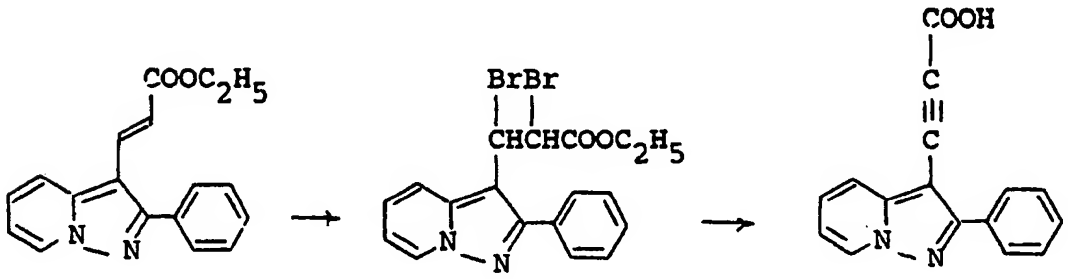
mp : 167-168° C

IR (Nujol) : 1705, 1640, 1620, 1500 cm^{-1}

NMR (DMSO-d_6, δ) : 3.17-3.87 (4H, m), 7.18 (1H, t, J=7.0Hz), 7.43-7.80 (6H, m), 8.27 (1H, d, J=9.0Hz), 8.85 (1H, d, J=7.0Hz)

Analysis Calcd. for $C_{17}H_{14}N_2O_3$ (%)	
Found :	C 69.37, H 4.80, N 9.52 C 69.63, H 4.51, N 9.63

Preparation 3



Bromine (13.86 g) was added dropwise to a solution of ethyl 3-(2-phenylpyrazolo[1,5-a]pyridin-3-yl)-acrylate (trans isomer) (25.30 g) in methylene chloride (250 ml) under ice-cooling with stirring. After being stirred for 2 hours, the reaction mixture was washed with an aqueous solution of sodium thiosulfate and saturated aqueous solution of sodium sulfate, dried over magnesium sulfate and evaporated in vacuo. The residue was recrystallized from ethyl acetate to give crystals of ethyl 2,3-dibromo-3-(2-phenylpyrazolo[1,5-a]pyridin-3-yl)propionate (26.33 g). This compound (13.80 g) was added to a solution of potassium hydroxide (85%, 9.09 g) in 95% ethanol (50 ml) at 70° C with stirring. The reaction mixture was heated under reflux for 6 hours. Ethanol was evaporated in vacuo. Water was added to the residue and the mixture was acidified with concentrated hydrochloric acid. The precipitates were collected by filtration, washed with ethanol and dried to give crystals of 3-(2-phenylpyrazolo[1,5-a]pyridin-3-yl)propiolic acid (3.35 g).

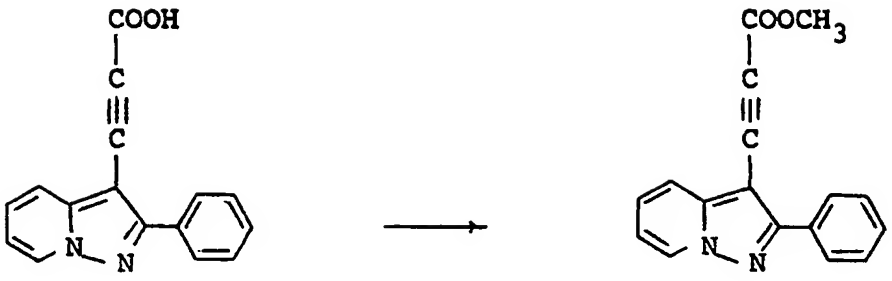
mp : >250° C

IR (Nujol) : 2200, 1685, 1630 cm^{-1}

NMR (DMSO-d_6, δ) : 7.08-8.43 (8H, m), 8.93 (1H, d, J=7.5Hz)

MS : 262 (M^+)

Preparation 4



3-(2-Phenylpyrazolo[1,5-a]pyridin-3-yl)propiolic acid (10.33 g) was added to a mixture of sodium hydroxide (3.15 g) and 95% ethanol (103 g), and then dimethyl sulfate (4.97 g) was added to the mixture. The reaction mixture was heated at 60 to 80°C for 3 hours and 20 minutes. Ethanol was evaporated in vacuo. Water was added to the residue and extracted with chloroform (50 ml x 3). Combined extract was washed with a saturated aqueous solution of sodium chloride (50 ml), dried over magnesium sulfate and evaporated in vacuo. The residue was recrystallized from ethyl acetate to give crystals of methyl 3-(2-phenylpyrazolo[1,5-a]pyridin-3-yl)propiolate (5.25 g).

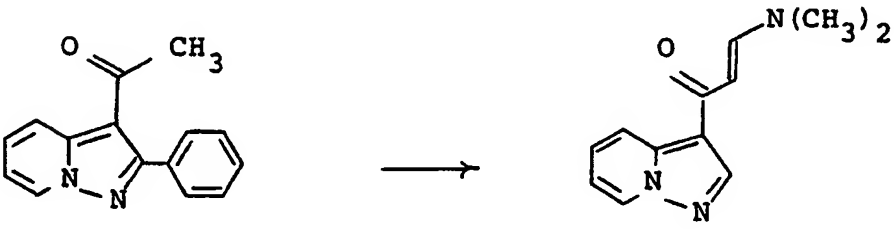
mp : 145-148°C

IR (Nujol) : 2190, 1700, 1630 cm^{-1}

NMR (DMSO-d_6, δ) : 3.78 (3H, s), 7.13 (1H, t, J=6.5Hz), 7.42-8.25 (7H, m), 8.83 (1H, d, J=6.5Hz)

Analysis Calcd. for $C_{17}H_{12}N_2O_2$ (%)	
Found :	C 73.90, H 4.38, N 10.14 C 73.94, H 4.36, N 10.17

Preparation 5



A mixture of 3-acetyl-2-phenylpyrazolo[1,5-a]pyridine (2.36 g), N,N-dimethylformamide dimethyl acetal (11.19 g) and 1,8-diazabicyclo[5.4.0]-7-undecene (1.50 g) was refluxed for 18 hours, and then the solvent was evaporated. To the residue, water (30 ml) was added. The solution thus obtained was extracted with chloroform (30 ml). The organic layer was evaporated. The residue was subjected to column chromatography on alumina (25 g) and eluted with a mixture of chloroform and n-hexane. The fractions containing the object compound were combined and concentrated in vacuo. The residue was recrystallized from chloroform and n-hexane to give 3-(3-N,N-dimethylaminoacryloyl)-2-phenylpyrazolo[1,5-a]pyridine (0.90 g).

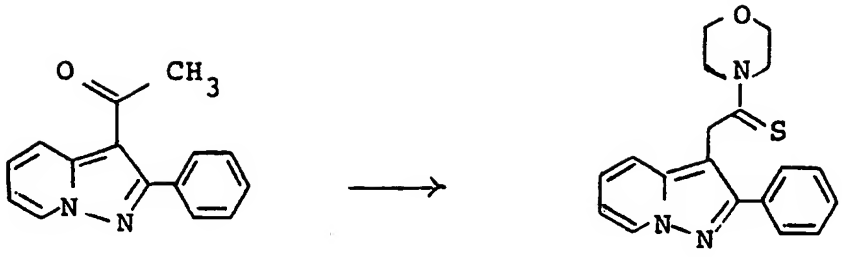
mp : 102-102.5°C

IR (Nujol) : 1620, 1585, 1540, 1500 cm^{-1}

NMR ($CDCl_3$, δ) : 2.67 (6H, s), 5.02 (1H, d, J=13Hz), 6.75 (1H, td, J=7Hz and 1Hz), 7.15-7.79 (6H, m), 8.33 (1H, d, J=8Hz), 8.42 (1H, d, J=7Hz)

MS : 291 (M^+)

Preparation 6



A mixture of 3-acetyl-2-phenylpyrazolo[1,5-a]pyridine (5.40 g), sulfur powder (2.20 g) and morpholine (10.8 ml) was refluxed for 24 hours. The reaction mixture was evaporated in vacuo and the residue was chromatographed on silica gel (80 g) with n-hexane-ethyl acetate (2:1) as an eluent. The fractions containing the object compound were combined and evaporated in vacuo to give 3-(2-morpholino-2-thioxoethyl)-2-phenylpyrazolo[1,5-a]pyridine. One recrystallization from a mixture of ethyl acetate and 2-propanol gave the crystals (5.50 g).

mp : 120-122 °C

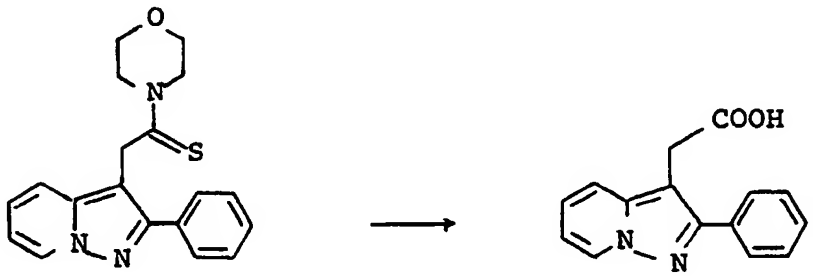
IR (Nujol) : 1630, 1530 cm^{-1}

NMR ($CDCl_3$, δ) : 3.05 (2H, t, J=5Hz), 3.28 (2H, t, J=5.0Hz), 3.58 (2H, t, J=5.0Hz), 4.25 (2H, t, J=5.0Hz), 4.53 (2H, s), 6.74 (1H, t, J=7.0Hz), 7.10 (1H, t, J=7.0Hz), 7.35-7.70 (5H, m), 8.05 (1H, d, J=9.0Hz), 8.42 (1H, d, J=7.0Hz)

MS : 334 (M^+), 203

Analysis Calcd. for $C_{19}H_{17}N_3OS$ (%)	
Found :	C 67.63, H 5.68, N 12.45 C 67.87, H 5.75, N 12.46

Preparation 7



A mixture of 3-(2-morpholino-2-thioxoethyl)-2-phenylpyrazolo[1,5-a]pyridine (5.50 g), potassium hydroxide (85%, 6.45 g) and water (44 ml) was refluxed for 14 hours. After cooling, the reaction mixture was poured onto ice (110 g) and acidified with 6N-hydrochloric acid (pH ≒ 2) and the resulting precipitates were collected to give 2-(2-phenylpyrazolo[1,5-a]pyridin-3-yl)acetic acid (4.20 g).

mp : 202-204 °C

IR (Nujol) : 1695, 1635 cm^{-1}

NMR (DMF-d_7, δ) : 3.85 (2H, s), 6.90 (1H, t, J=7.5Hz), 7.23 (1H, t, J=7.5Hz), 7.37-8.00 (6H, m), 8.65 (1H, d, J=7.5Hz)

MS : 252 (M^+), 221, 207

Preparation 8

Phosphorus oxychloride (27.6 g) was added dropwise to N,N-dimethylformamide (16.6 ml) for 20 minutes under ice-cooling, 2-(2-phenylpyrazolo[1,5-a]pyridin-3-yl)acetic acid (9.08 g) was added to the solution thus obtained and the reaction mixture was stirred at 90-100°C for 20 hours. After cooling, the reaction mixture was poured onto ice (20 g). The mixture was made alkaline with 24% aqueous solution of sodium hydroxide (pH ≒ 9) and stirred at 90°C for 1 hour and 20 minutes. After cooling, the resulting mixture was extracted with ethyl acetate three times. The combined extract was washed with water and dried over magnesium sulfate. The solvent was removed and recrystallized from a mixture of ethyl acetate and isopropanol to give 3-(N,N-dimethylamino)-2-(2-phenylpyrazolo[1,5-a]pyridin-3-yl)acrylaldehyde (cis and trans mixture) (5.00 g).

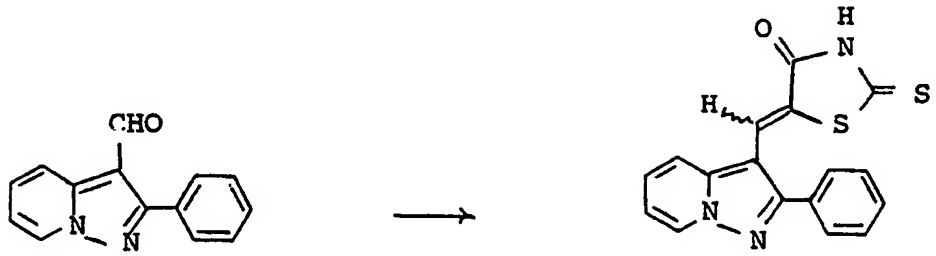
mp : 154-155°C

IR (Nujol) : 2710, 1590, 1580 cm^{-1}

NMR ($CDCl_3$, δ) : 2.70 (6H, m), 6.70 (1H, t, J=7.5Hz), 6.90-7.47 (6H, m), 7.70-7.95 (2H, m), 8.40 (1H, d, J=7.5Hz), 9.19 (1H, s)

MS : 291 (M^+), 274, 232, 218

Preparation 9



A mixture of 2-phenylpyrazolo[1,5-a]pyridine-3-carbaldehyde (15.0 g), rhodanine (9.44 g), sodium acetate (16.6 g) and glacial acetic acid (90 ml) was refluxed for 10 hours. Water(200 ml) and ethyl acetate (90 ml) were added to the reaction mixture and the resulting precipitates were collected by filtration to give 5-(2-phenylpyrazolo[1,5-a]pyridin-3-yl)methylenerhodanine (cis and trans mixture) (19.8 g).

mp : 312-314°C

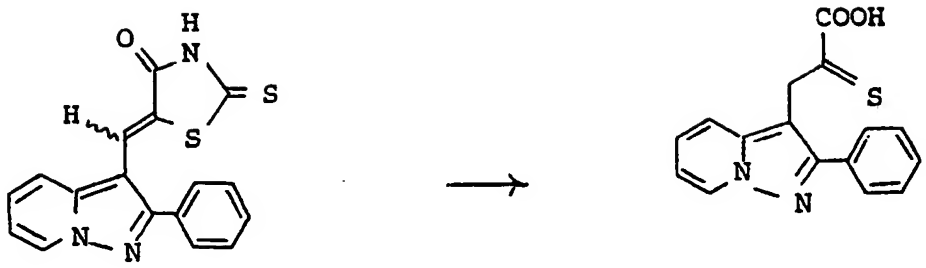
IR (Nujol) : 1685, 1590 cm^{-1}

NMR (DMSO-d_6, δ) : 7.20 (1H, t, J=6.8Hz), 7.51-7.68 (6H, m), 7.98 (1H, s), 7.95 (1H, d, J=8.9Hz), 8.91 (1H, d, J=6.9Hz), 13.6 (1H, broad)

MS : 337 (M^+), 250, 218

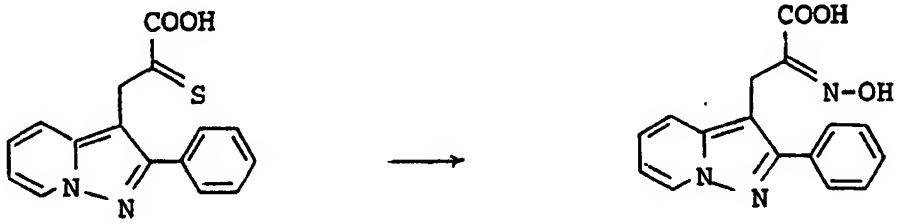
Analysis Calcd. for $C_{17}H_{11}N_3OS_2$ (%)	
Found :	C 60.52, H 3.29, N 12.45 C 60.58, H 3.25, N 12.38

Preparation 10



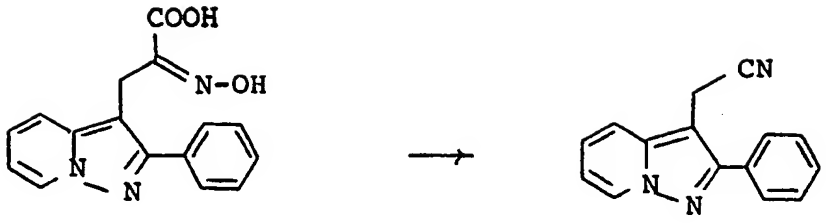
A mixture of 5-(2-phenylpyrazolo[1,5-a]pyridin-3-yl)methylenerhodanine (13.0 g) and 15% aqueous solution of sodium hydroxide (50 ml) was refluxed for 3 hours. To the reaction mixture was added 10% hydrochloric acid (50 ml) and water (50 ml) and was stirred for an hour under ice-cooling. The precipitates were collected by filtration to give 3-(2-phenylpyrazolo[1,5-a]pyridin-3-yl)-2-thioxopropionic acid (7.85 g).
mp : 199-201 °C
IR (Nujol) : 1690, 1625, 1590, 1570 cm^{-1}
NMR (DMF-d_7, δ) : 7.02 (1H, t, J=7.5Hz), 6.8-8.3 (10H, m), 8.68 (1H, d, J=7.5Hz)
MS : 296 (M^+), 250, 219, 194

Preparation 11



A mixture of 3-(2-phenylpyrazolo[1,5-a]pyridin-3-yl)-2-thioxopropionic acid (3.74 g), hydroxylamine hydrochloride (2.63 g), 85% potassium hydroxide (2.50 g) and 80% aqueous ethanol (22.4 ml) was refluxed for 3 hours. After cooling, to the reaction mixture was added water (40 ml) and the resulting precipitates were filtered off. The filtrate was washed with methylene chloride (20 ml) twice, acidified with 10% aqueous hydrochloric acid (pH ≒ 2), and extracted with ethyl acetate (20 ml) twice. The organic layer was washed with water (10 ml) and a saturated aqueous solution of sodium chloride and dried over magnesium sulfate. The solvent was removed to give 3-(2-phenylpyrazolo[1,5-a]pyridin-3-yl)-2-hydroxyiminopropionic acid (2.60 g).
IR (Nujol) : 3400-3000, 1680, 1635 cm^{-1}
NMR (DMF-d_7, δ) : 4.00 and 4.20 (total 2H, each s), 6.70-8.03 (9H, m), 8.55 (1H, d, J=7.5Hz)

Preparation 12



A solution of 3-(2-phenylpyrazolo[1,5-a]pyridin-3-yl)-2-hydroxyiminopropionic acid (0.20 g) in acetic anhydride (1 ml) was stirred for an hour at 80 °C. After cooling, to the mixture was added water (10 ml). The resulting precipitates were collected by filtration to give 2-(2-phenylpyrazolo[1,5-a]pyridin-3-yl)acetonitrile (0.10 g).

mp : 111-114 °C

IR (Nujol) : 2245, 1630, 1525 cm^{-1}

NMR ($CDCl_3$, δ) : 3.93 (2H, s), 6.85 (1H, t, J=7.5Hz), 7.24 (1H, t, J=7.5Hz), 7.37-7.78 (6H, m), 8.50 (1H, d, J=7.5Hz)

MS : 233, 207

Preparation 13

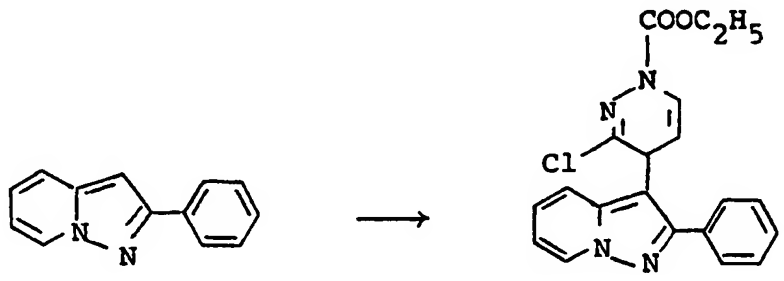
A mixture of 2-(2-phenylpyrazolo[1,5-a]pyridin-3-yl)acetonitrile (0.23 g), 85% sodium hydroxide (0.33 g) and 80% aqueous methanol was refluxed for 15 hours. The reaction mixture was acidified with 5% hydrochloric acid (pH ≒ 1) and the precipitates were collected by filtration to give 2-(2-phenylpyrazolo[1,5-a]pyridin-3-yl)acetic acid (0.23 g).

mp : 197-201 °C

IR (Nujol) : 1700, 1630 cm^{-1}

NMR (DMSO-d_6, δ) : 3.86 (2H, s), 6.88 (1H, t, J=7.5Hz), 7.21 (1H, t, J=7.0Hz), 7.35-7.83 (6H, m), 8.64 (1H, d, J=7.5Hz), 11.8-12.8 (1H, broad s)

Example 8



To a mixture of 3-chloropyridazine (0.66 g), 2-phenylpyrazolo[1,5-2]pyridine (1.12 g) and chloroform (6.6 ml) was added ethyl chloroformate (1.38 g) under ice-cooling and stirred for 2 hours at room temperature.

To the reaction mixture was added methylene chloride (10 ml). The solution was washed with a saturated aqueous solution of sodium hydrogen carbonate (10 ml), and dried over magnesium sulfate. The organic layer was evaporated in vacuo and recrystallized from a mixture of ethyl acetate and 2-propanol to give 3-(3-chloro-1-ethoxycarbonyl-1,4-dihydropyridazin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine (1.60 g).

mp : 129.5-131.5 °C

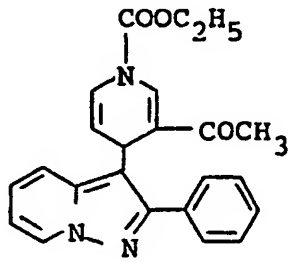
IR (Nujol) : 1715, 1675, 1630 cm^{-1}

NMR ($CDCl_3$, δ) : 1.42 (3H, t, J=7.1Hz), 4.42 (2H, q, J=7.1Hz), 4.80 (1H, dd, J=1.6Hz and 3.6Hz), 5.00 (1H, dd, J=3.6Hz and 8.2Hz), 6.86 (1H, dt, J=1.4Hz and 6.8Hz), 7.15-7.69 (8H, m), 8.51 (1H, dd, J=1.0Hz and 7.0Hz)

Analysis Calcd. for $C_{20}H_{17}ClN_4O_2$ (%)	
Found :	C 63.08, H 4.50, N 14.71 C 63.04, H 4.52, N 14.50

The following compounds (Examples 9 and 10) were obtained according to a similar manner to that of Example 8.

Example 9



3-(3-Acetyl-1-ethoxycarbonyl-1,4-dihydropyridin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine

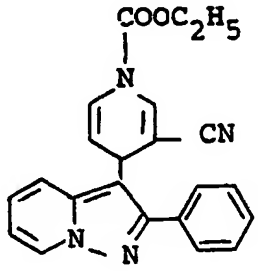
mp : 151-153 °C

IR (Nujol) : 1735, 1660, 1610 cm^{-1}

NMR ($CDCl_3$, δ) : 1.32 (3H, t, J=7.5Hz), 2.05 (3H, s), 4.32 (2H, q, J=7.5Hz), 4.84 (1H, d, J=4.0Hz), 5.15 (1H, dd, J=8.0Hz and 4.0Hz), 6.75 (1H, d, J=8.0Hz), 6.80 (1H, t, J=7.5Hz), 7.15 (1H, t, J=7.5Hz), 7.16-7.75 (6H, m), 7.82 (1H, s), 8.58 (1H, d, J=7.5Hz)

MS : 387 (M^+), 344, 314, 300, 269, 241

Example 10



3-(3-Cyano-1-ethoxycarbonyl-1,4-dihydropyridin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine

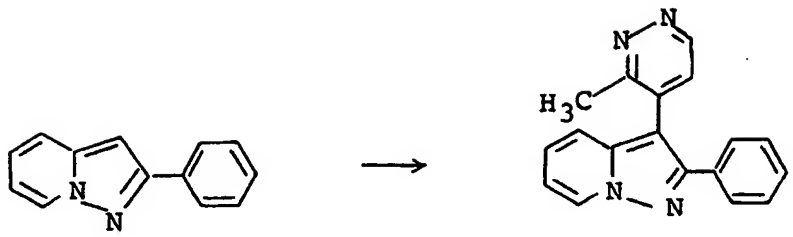
mp : 182-183 °C

IR (Nujol) : 2215, 1740, 1680, 1620 cm^{-1}

NMR ($CDCl_3$, δ) : 1.31 (3H, t, J=7.5Hz), 4.29 (2H, q, J=7.5Hz), 4.75 (1H, m), 5.14 (1H, dd, J=9.0Hz and 3.0Hz), 6.80 (1H, d, J=9.0Hz), 6.93 (1H, t, J=7.5Hz), 7.27 (1H, t, J=7.5Hz), 7.36-7.70 (7H, m), 8.70 (1H, d, J=7.5Hz)

MS : 370 (M^+), 342, 325, 297, 270

Example 11



To a mixture of 2-phenylpyrazolo[1,5-a]pyridine (5.00 g), 3-methylpyridazine (2.90 g) and methylene chloride (20 ml), was added a solution of ethyl chloroformate (5.57 g) in methylene chloride for 17 minutes under ice-cooling and stirred for an hour at the same temperature and then for 6 hours and 40 minutes at room temperature. To the reaction mixture was added methylene chloride (20 ml), and washed with a solution of potassium carbonate (10 ml) and a saturated aqueous solution of sodium chloride (10 ml) and dried over magnesium sulfate. The solvent was removed and chromatographed on silica gel (70 g) with a mixture of n-hexane and ethyl acetate (2:1). The fractions containing the object compound were combined and evaporated in vacuo and recrystallized from a mixture of ethyl acetate and n-hexane to give 3-(3-methylpyridazin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine (2.36 g).

mp : 209-214 °C

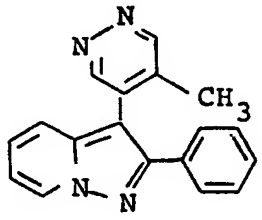
IR (Nujol) : 1630, 1610 cm^{-1}

NMR ($CDCl_3$, δ) : 246 (3H, s), 6.98 (1H, t, J=7.5Hz), 7.19-7.58 (7H, m), 7.91 (1H, d, J=6.0Hz), 8.58 (1H, d, J=7.5Hz), 9.32 (1H, d, J=6.0Hz)

MS : 286 (M^+), 257, 231, 218

The following compounds (Examples 12 and 13) were obtained according to a similar manner to that of Example 11.

Example 12



3-(5-Methylpyridazin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine

mp : 158-159.5 °C

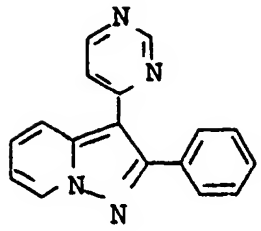
IR (Nujol) : 3080, 1630 cm^{-1}

NMR ($CDCl_3$, δ) : 1.90 (3H, s), 6.80 (1H, t, J=7.5Hz), 7.12-7.50 (7H, m), 8.51 (1H, d, J=7.5Hz), 8.99 (2H, s)

MS : 286 (M^+), 257, 243, 218

Analysis Calcd. for $C_{18}H_{14}N_4$ (%)	
Found :	C 75.50, H 4.93, N 19.57 C 75.22, H 5.09, N 19.26

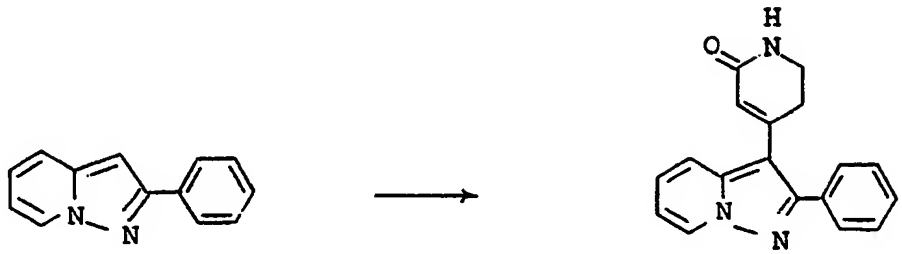
Example 13



3-(Pyrimidin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine mp : 130-131 °C
IR (Nujol) : 1625, 1580 cm^{-1}
NMR ($CDCl_3$, δ) : 696-7.06 (2H, m), 7.35-7.64 (6H, m), 8.40 (1H, d, J=5.4Hz), 8.22-8.61 (2H, m), 9.22 (1H, d, J=1.3Hz)
MS : 271 (M^+), 244, 217

Analysis Calcd. for $C_{17}H_{12}N_4$ (%)	
Found :	C 74.98, H 4.44, N 20.57 C 74.87, H 4.62, N 20.33

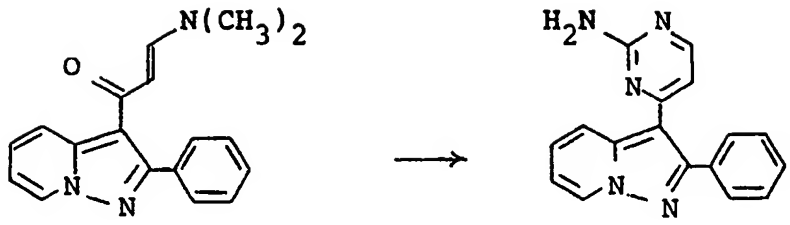
Example 14



A mixture of 2-phenylpyrazolo[1,5-a]pyridine (0.50 g), 2,4-piperidinedione (0.292 g), concentrated sulfuric acid (1 drop) and acetic acid (0.5 ml) was heated at 135 °C for 13.5 hours. A saturated aqueous solution of sodium hydrogen carbonate (20 ml) was added to the reaction mixture and the mixture was extracted with chloroform (20 ml x 2). The combined extract was washed with a saturated aqueous solution of sodium chloride (20 ml) and dried over magnesium sulfate. The solvent was evaporated in vacuo. The residue was purified by column chromatography on silica gel using a mixture of chloroform and ethyl acetate (9:1) and recrystallized from ethyl acetate to give crystals of 3-(2-oxo-1,2,5,6-tetrahydropyridin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine.
mp : 188 to 189 °C
IR (Nujol) : 1655, 1630, 1605 cm^{-1}
NMR ($CDCl_3$, δ, 6) : 2.44 (2H, t, J=6.5Hz), 3.44 (2H, t, J=6.5Hz), 6.20 (2H, s), 6.86 (1H, td, J=7.0Hz and 1.0Hz), 7.20-7.75 (7H, m), 8.50 (1H, dt, J=7.0Hz and 1.0Hz)

Analysis Calcd. for $C_{18}H_{15}N_3O$ (%)	
Found :	C 74.72, H 5.23, N 14.53 C 75.13, H 5.33, N 14.69

Example 15



A solution of 3-(3-N,N-dimethylaminoacryloyl)-2-phenylpyrazolo[1,5-a]pyridine (0.63 g), guanidine hydrochloride (0.31 g), sodium ethoxide (0.54 g) and ethanol (9 ml) was refluxed for 2 hours. To the reaction mixture water (30 ml) was added and the mixture was extracted with ethyl acetate (60 ml). The organic layer was evaporated, then that residue was recrystallized from ethanol to give 3-(2-aminopyrimidin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine (0.40 g).

mp : 222.5-223 °C

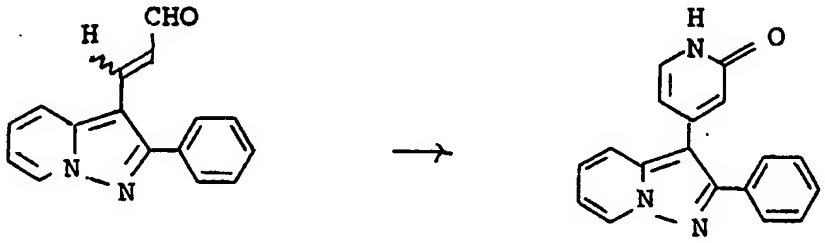
IR (Nujol) : 3370, 3320, 3180, 1640, 1560 cm^{-1}

NMR ($CDCl_3$, δ) : 6.14 (1H, d, J=4.8Hz), 6.52 (2H, s), 7.05(1H, td, J=7Hz and 1Hz), 8.53 (1H, d, J=8Hz), 8.76 (1H, d, J=7Hz)

MS : 286

Analysis Calcd. for $C_{17}H_{13}N_5$ (%)	
Found :	C 71.07, H 4.56, N 24.37 C 70.93, H 4.59, N 23.74

Example 16



A mixture of 3-(2-phenylpyrazolo[1,5-a]pyridin-3-yl)acrylaldehyde (cis and trans mixture) (1.15 g) and 1-carbamoylmethylpyridinium chloride (0.80 g), 50% aqueous dimethylamine (0.44 g) and methanol (10 ml) was refluxed for 3 hours. The reaction mixture was evaporated in vacuo and the residue was heated for 10 minutes at 200 °C. The resulting mixture was chromatographed on silica gel (80 g) with a mixture of chloroform and methanol (100:1). The fractions containing the object compound were combined and evaporated in vacuo and recrystallized from ethanol to give 3-(2-oxo-1,2-dihydropyridin-4-yl)-2-phenylpyrazolo [1,5-a]pyridine (0.33 g).

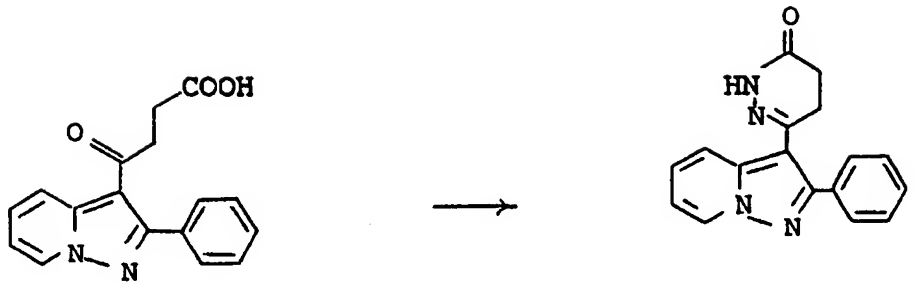
IR (Nujol) : 1655, 1580 cm^{-1}

NMR (DMSO-d_6, δ) : 5.72 (1H, dd, J=1.8Hz and 6.8Hz), 6.30 (1H, d, J=1.2Hz), 7.04 (1H, dt, J=1.3Hz and 6.8Hz), 7.33-7.62 (7H, m), 7.73 (1H, d, J=9.0Hz), 8.80 (1H, d, J=7.0Hz), 11.52 (1H, broad s)

MS : 286 (M^+-1), 268

Analysis Calcd. for $C_{18}H_{13}N_3O \cdot 1/3H_2O$ (%)	
Found :	C 73.60, H 4.69, N 14.30 C 73.70, H 4.82, N 14.28

Example 17



A mixture of 4-oxo-4-(2-phenylpyrazolo[1,5-a]pyridin-3-yl)butyric acid (1.71 g), hydrazine monohydrate (1.46 g) and ethanol (17 ml) was heated under reflux for 1 hour. Ethanol was evaporated in vacuo. Water (20 ml) was added to the residue, acidified with 5% hydrochloric acid and extracted with chloroform (25 ml x 3). The combined extract was washed with a saturated aqueous solution of sodium chloride, dried over magnesium sulfate and evaporated in vacuo. The residue was recrystallized from ethanol to give crystals of 3-(3-oxo-2,3,4,5-tetrahydropyridazin-6-yl)-2-phenylpyrazolo[1,5-a]pyridine (1.19 g).

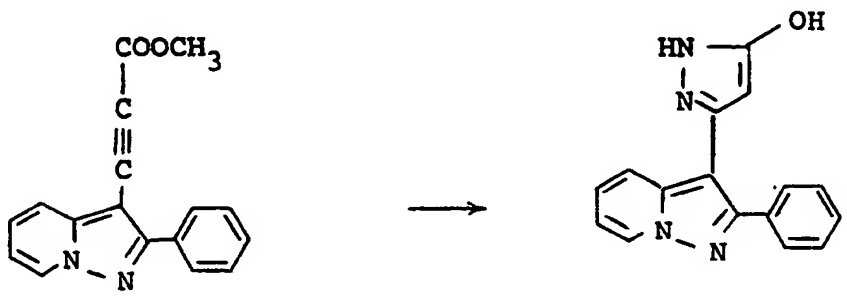
mp : 187 to 189 °C

IR (Nujol) : 3325, 1675, 1630 cm^{-1}

NMR (DMSO-d_6, δ) : 2.29-2.51 (4H, m), 7.05 (1H, td, J=7.0Hz and 1.0Hz), 7.37-7.68 (6H, m), 7.96 (1H, d, J=9.0Hz), 8.78 (1H, d, J=7.0Hz)

Analysis Calcd. for $C_{17}H_{14}N_4O$ (%)	
Found :	C 70.33, H 4.86, N 19.30 C 70.27, H 4.72, N 19.17

Example 18



A mixture of methyl 3-(2-phenylpyrazolo[1,5-a]pyridin-3-yl)propiolate (1.50 g), hydrazine monohydrate (0.544 g) and ethanol (15 ml) was heated under reflux for 2 hours. Ethanol was evaporated in vacuo. Water (50 ml) was added to the residue and the mixture was acidified with 1N hydrochloric acid. The resultant precipitates were collected by filtration and washed with water. Recrystallization from a mixture of N,N-dimethylformamide and water gave crystals of 3-(5-hydroxypyrazol-3-yl)-2-phenylpyrazolo[1,5-a]pyridine (0.64 g).

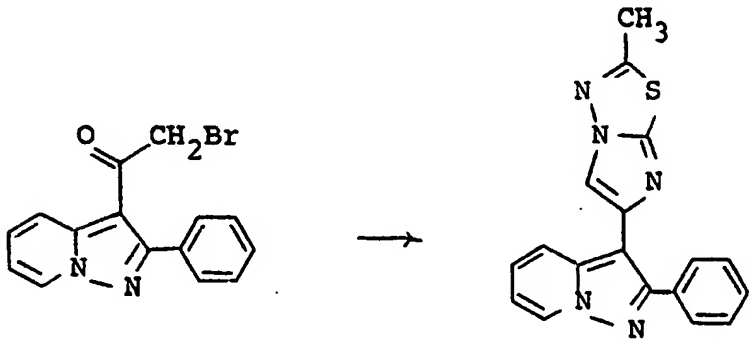
mp : >300°C

IR (Nujol) : 2670, 2570, 1640, 1610 cm^{-1}

NMR (DMSO-d_6, δ) : 5.43 (1H, s), 6.97 (1H, td, J=7.0Hz and 1.0Hz), 7.21-7.80 (7H, m), 8.73 (1H, d, J=7.0Hz)

Analysis Calcd. for $C_{16}H_{12}N_4O$ (%)	
Found :	C 69.55, H 4.38, N 20.28 C 69.46, H 4.35, N 19.99

Example 19



A mixture of 3-(2-bromoacetyl)-2-phenylpyrazolo[1,5-a]pyridine (1.87 g), 2-amino-5-methyl-1,3,4-thiadiazole (0.68 g) and 1-butanol (19 ml) was refluxed for 5 hours and 20 minutes. The reaction mixture was evaporated in vacuo and the residue was taken up methylene chloride (40 ml). The methylene chloride solution was washed with an aqueous solution of potassium carbonate and dried over magnesium sulfate. The solvent was removed and the residue was subjected to chromatography on silica gel (25 g) with chloroform as an eluent. The fractions containing the objective compound were combined and evaporated in vacuo to give 3-(2-methylimidazo[2,1-b][1,3,4]thiadiazol-6-yl)-2-phenylpyrazolo[1,5-a]pyridine (1.06 g), which was recrystallized from acetone gave crystals (0.69 g).

mp : 204°C

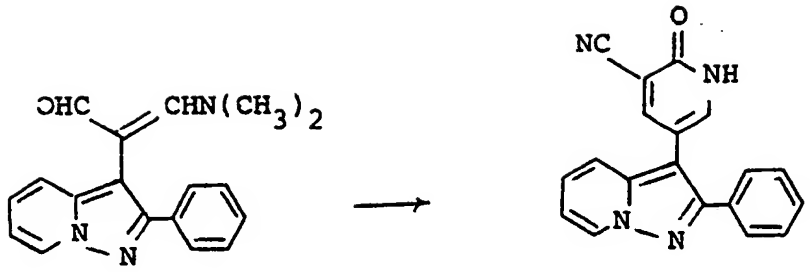
IR (Nujol) : 3130, 3100, 1635, 1590 cm^{-1}

NMR ($CDCl_3$, δ) : 2.65 (3H, s), 6.75 (1H, t, J=7.5Hz), 7.13 (1H, t, J=7.5Hz), 7.25-7.50 (4H, m), 7.55-7.80 (2H, m), 8.14 (1H, d, J=9.0Hz), 8.40 (1H, d, J=7.5Hz)

MS : 302 (M^+), 261, 221, 193

Analysis Calcd. for $C_{18}H_{13}N_3S$ (%)	
Found :	C 62.24, H 3.95, N 21.13 C 65.58, H 3.98, N 21.25

Example 20



A mixture of 3-(N,N-dimethylamino)-2-(2-phenylpyrazolo[1,5-a]pyridin-3-yl)acrylaldehyde (cis and trans mixture) (4.00 g), 2-cyanoacetamide (2.31 g), sodium ethoxide (4.67 g) and ethanol (40 ml) was refluxed for 2 hours. After cooling the reaction mixture was added acetic anhydride (24 ml) and water (120 ml) and stirred at room temperature. The resultant precipitates were collected and recrystallized from a mixture of N,N-dimethylformamide and water to give 3-(3-cyano-2-oxo-1,2-dihydropyridin-5-yl)-2-phenylpyrazolo[1,5-a]-pyridine (2.08 g).

mp : 312-314°C

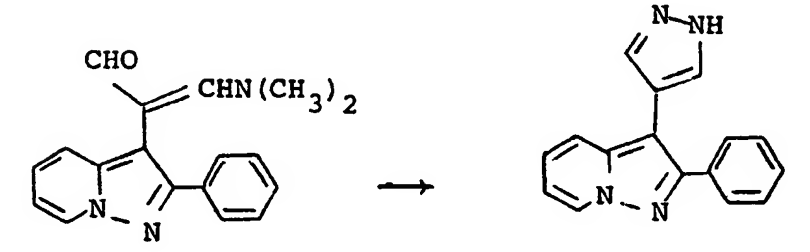
IR (Nujol) : 2240, 1670, 1540 cm^{-1}

NMR (DMSO-d_6, δ) : 6.93 (1H, t, J=7.5Hz), 7.27 (1H, t, J=7.5Hz), 7.33-7.72 (8H, m), 8.03 (1H, d, J=7.5Hz), 8.71 (1H, d, J=7.5Hz)

MS : 312 (M^+), 283

Analysis Calcd. for $C_{19}H_{12}N_4O$ (%)	
Found :	C 73.07, H 3.87, N 17.94 C 72.96, H 4.19, N 17.83

Example 21



A mixture of 3-(N,N-dimethylamino)-2-(2-phenylpyrazolo[1,5-a]pyridin-3-yl)acrylaldehyde (0.70 g), hydrazine mono hydrate (0.18 g) and ethanol (7 ml) was refluxed for 4 hours. To the reaction mixture was added water (12 ml), and stirred under ice-cooling. The precipitates were collected and recrystallized from a mixture of ethanol and water to give 3-(4-pyrazolyl)-2-phenylpyrazolo[1,5-a]pyridine (0.51 g).

mp : 188-190°C

IR (Nujol) : 3150, 1630 cm^{-1}

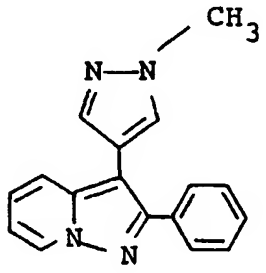
NMR ($CDCl_3$, δ) : 6.75 (1H, t, J=7.5Hz), 7.10 (1H, t, J=7.5Hz), 7.25-7.80 (9H, m), 8.57 (1H, d, J=7.5Hz)

MS : 260 (M^+), 232, 205

Analysis Calcd. for $C_{16}H_{12}N_4$ (%)	
Found :	C 73.83, H 4.65, N 21.52 C 73.49, H 5.01, N 21.18

The following compounds (Examples 22 to 25) were obtained according to a similar manner to that of Example 21.

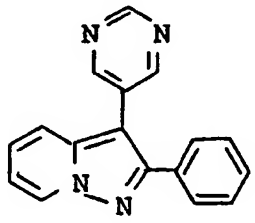
Example 22



3-(1-Methylpyrazol-4-yl)-2-phenylpyrazolo[1,5-a]pyridine
mp : 100-103 °C
IR (Nujol) : 1630 cm^{-1}
NMR ($CDCl_3$, δ) : 3.90 (3H, s), 6.70 (1H, t, J=7.5Hz), 7.07 (1H, t, J=7.5Hz), 7.21-7.46 (5H, m), 7.48 (1H, s), 7.60-7.80 (2H, m), 8.43 (1H, d, J=7.5Hz)
MS : 274 (M^+), 246

Analysis Calcd. for $C_{17}H_{14}N_4$ (%)	
Found :	C 74.43, H 5.14, N 20.42 C 74.64, H 5.46, N 20.36

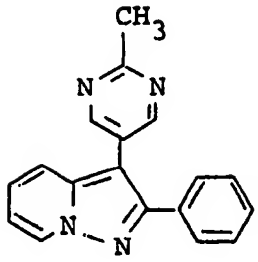
Example 23



3-(5-Pyrimidinyl)-2-phenylpyrazolo[1,5-a]pyridine mp : 163-165 °C
IR (Nujol) : 1625 cm^{-1}
NMR ($CDCl_3$, δ) : 6.83 (1H, t, J=7.5Hz), 7.18 (1H, t, J=7.5Hz), 7.25-7.60 (6H, m), 8.51 (1H, d, J=7.5Hz), 8.70 (2H, s), 9.10 (1H, s)
MS : 272 (M^+), 244, 218

Analysis Calcd. for $C_{17}H_{12}N_4$ (%)	
Found :	C 74.98, H 4.44, N 20.57 C 75.14, H 5.04, N 20.42

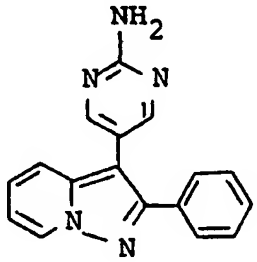
Example 24



3-(2-Methylpyrimidin-5-yl)-2-phenylpyrazolo[1,5-a]pyridine
mp : 152-153° C
IR (Nujol) : 3030-3100, 1635 cm^{-1}
NMR ($CDCl_3$, δ) : 2.73 (3H, s), 6.80 (1H, t, J=7.5Hz), 7.18 (1H, t, J=7.5Hz), 7.20-7.65 (6H, m), 8.50 (1H, d, J=7.5Hz), 8.60 (2H, s)
MS : 286 (M^+), 244, 218

Analysis Calcd. for $C_{18}H_{14}N_4$ (%)	
Found :	C 75.51, H 4.93, N 19.57 C 75.38, H 5.14, N 19.16

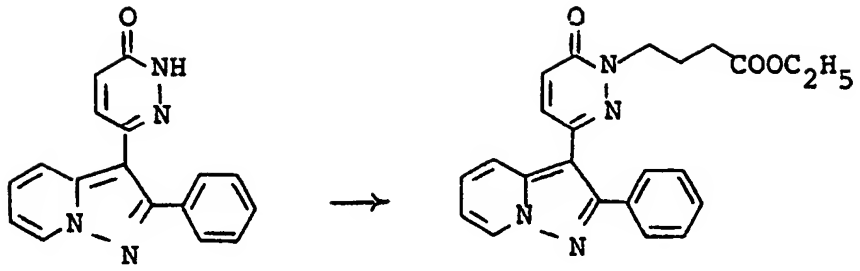
Example 25



3-(2-Aminopyrimidin-5-yl)-2-phenylpyrazolo[1,5-a]pyridine
mp : 304-305° C
IR (Nujol) : 3400-3050, 1660, 1605 cm^{-1}
NMR (DMSO-d_6, δ) : 6.43 (2H, s), 6.68 (1H, t, J=7.5Hz), 7.02 (1H, t, J=7.5Hz), 7.07-7.45 (6H, m), 7.93 (2H, s), 8.48 (1H, d, J=7.5Hz)
MS : 287 (M^+), 246, 218

Analysis Calcd. for $C_{17}H_{13}N_5$ (%)	
Found :	C 71.07, H 4.56, N 24.37 C 71.23, H 4.88, N 24.04

Example 26



A mixture of 3-(3-oxo-2,3-dihydropyridazin-6-yl)-2-phenylpyrazolo[1,5-a]pyridine (0.47 g), ethyl 4-bromobutyrate (0.32 g), triton B (0.5 ml) and chloroform was stirred for 2 days under room temperature. The reaction mixture was evaporated and the residue was subjected to a column chromatography on silica gel (20 g) with chloroform as an eluent. The fractions containing the object compound were combined (20 ml) and concentrated under reduced pressure. The residue was dissolved in ethyl acetate and filtered off. The filtrate was evaporated to give 3-[2-(3-ethoxycarbonylpropyl)-3-oxo-2,3-dihydropyridazin-6-yl]-2-phenylpyrazolo[1,5-a]pyridine (0.49 g).

mp : 71-75 °C

IR (Nujol) : 1730, 1660, 1630, 1590, 1525 cm^{-1}

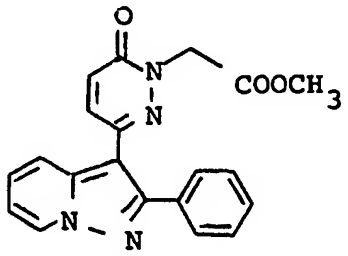
NMR ($CDCl_3$, δ, 6) : 1.25 (3H, t, J=6Hz), 2.00-2.60 (4H, m), 4.00-4.45 (4H, Hex), 6.77 (1H, d, J=10Hz), 6.92 (1H, td, J=7Hz and 1Hz), 7.03 (1H, d, J=10Hz), 7.25-7.80 (6H, m), 8.00 (1H, d, J=9Hz), 8.52 (1H, d, J=7Hz)

MS : 402

Analysis Calcd. for $C_{23}H_{22}N_4O_3$ (%)	
Found :	C 68.64, H 5.51, N 13.92 C 68.79, H 5.78, N 13.72

The following compounds (Examples 27 to 32) were obtained according to a similar manner to that of Example 26.

Example 27



3-(2-Methoxycarbonylmethyl-3-oxo-2,3-dihydropyridazin-6-yl)-2-phenylpyrazolo[1,5-a]pyridine

mp : 142.5-143 °C

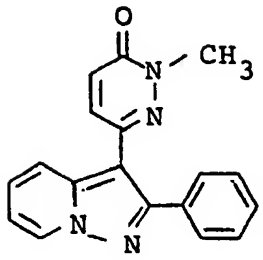
IR (Nujol) : 1740, 1670, 1630, 1590 cm^{-1}

NMR ($CDCl_3$, δ) : 3.82 (3H, s), 4.99 (2H, s), 6.75 (1H, d, J=10Hz), 6.87 (1H, td, J=7Hz and 1Hz), 7.03 (1H, d, J=10Hz), 7.18-7.75 (6H, m), 7.93 (1H, d, J=8Hz), 8.50 (1H, d, J=7Hz)

MS : 360 (M^+)

Analysis Calcd. for $C_{20}H_{16}N_4O_3$ (%)	
Found :	C 66.66, H 4.47, N 15.55 C 66.69, H 4.47, N 15.75

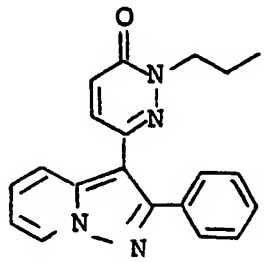
Example 28



3-(2-Methyl-3-oxo-2,3-dihydropyridazin-6-yl)-2-phenylpyrazolo[1,5-a]pyridine
mp : 145-145.5°C
IR (Nujol) : 1675, 1585, cm^{-1}
NMR ($CDCl_3$, δ) : 3.89 (3H, s), 6.72 (1H, d, J=9Hz), 6.88 (1H, td, J=6Hz and 1Hz), 7.00 (1H, d, J=9Hz), 7.15-7.70 (6H, m), 7.97 (1H, d, J=9Hz), 8.50 (1H, d, J=8Hz)
MS : 302

Analysis Calcd. for $C_{18}H_{14}N_4O$ (%)	
Found :	C 71.51, H 4.67, N 18.53 C 71.60, H 4.58, N 18.65

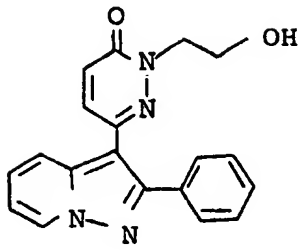
Example 29



3-(2-Propyl-3-oxo-2,3-dihydropyridazin-6-yl)-2-phenylpyrazolo[1,5-a]pyridine
mp : 110-110.5°C
IR (Nujol) : 1660, 1590, 1530 cm^{-1}
NMR ($CDCl_3$, δ) : 1.05 (3H, t, J=7Hz), 1.95 (2H, Hex, J=7Hz), 4.23 (2H, t, J=7Hz), 6.72 (1H, d, J=10Hz), 6.87 (1H, td, J=7Hz and 1Hz), 6.97 (1H, d, J=10Hz), 7.17-7.70 (6H, m), 7.93 (1H, d, J=10Hz), 8.50 (1H, d, J=7Hz)
MS : 330

Analysis Calcd. for $C_{20}H_{18}N_4O$ (%)	
Found :	C 72.71, H 5.49, N 16.96 C 72.81, H 5.65, N 16.98

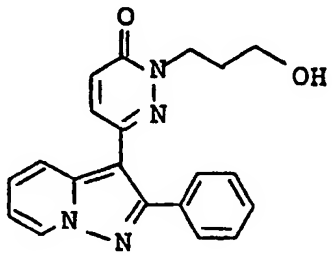
Example 30



3-[2-(2-Hydroxyethyl)-3-oxo-2,3-dihydropyridazin-6-yl]-2-phenylpyrazolo[1,5-a]pyridine
mp : 185.5-187°C
IR (Nujol) : 3350, 1650, 1580, 1520, 1500 cm^{-1}
NMR ($CDCl_3$, δ) : 4.05 (2H, m), 4.30 (2H, d, J=4Hz), 6.70 (1H, d, J=10Hz), 6.82 (1H, td, J=7Hz and 1Hz), 7.00 (1H, d, J=10Hz), 7.15-7.60 (6H, m), 7.87 (1H, d, J=10Hz), 8.45 (1H, d, J=7Hz)
MS : 332 (M^+)

Analysis Calcd. for $C_{19}H_{16}N_4O_2$ (%)	
Found :	C 68.66, H 4.85, N 16.86 C 67.29, H 5.05, N 16.42

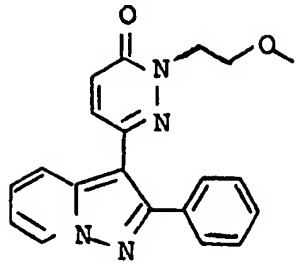
Example 31



3-[2-(3-Hydroxypropyl)-3-oxo-2,3-dihydropyridazin-6-yl]-2-phenylpyrazolo[1,5-a]pyridine
mp : 164.5-165°C
IR (Nujol) : 1660, 1590, 1540 cm^{-1}
NMR ($CDCl_3$, δ) : 2.11 (2H, g, J=6Hz), 3.46-3.70 (3H, m), 4.46 (2H, t, J=6Hz), 6.80 (1H, d, J=10Hz), 6.14 (1H, td, J=7Hz and 1Hz), 7.01 (1H, d, J=10Hz), 7.26-7.64 (6H, m), 7.99 (1H, d, J=8Hz)
MS : 346 (M^+)

Analysis Calcd. for $C_{20}H_{18}N_4O_2$ (%)	
Found :	C 69.35, H 5.24, N 16.17 C 69.02, H 5.28, N 15.74

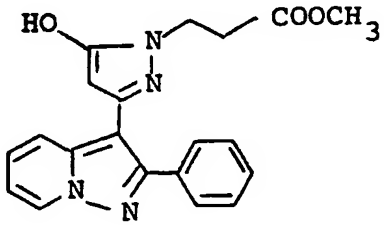
Example 32



3-[2-(2-Ethoxyethyl)-3-oxo-2,3-dihydropyridazin-6-yl]-2-phenylpyrazolo[1,5-a]pyridine
mp : 117-118 °C
IR (Nujol) : 1665, 1630, 1590, 1530 cm^{-1}
NMR ($CDCl_3$, δ) : 1.23 (3H, t, J=7Hz), 3.59 (2H, q, J=7Hz), 3.92 (2H, t, J=6Hz), 4.49 (2H, t, J=6Hz), 6.75 (1H, d, J=10Hz), 6.94 (1H, td, J=6Hz and 1Hz), 7.00 (1H, d, J=10Hz), 7.24-7.76 (6H, m), 8.12 (1H, d, J=12Hz), 8.52 (1H, d, J=8Hz)
MS 360 (M^+)

Analysis Calcd. for $C_{21}H_{20}N_4O_2$ (%)	
Found :	C 69.98, H 5.59, N 15.55 C 70.57, H 5.52, N 15.82

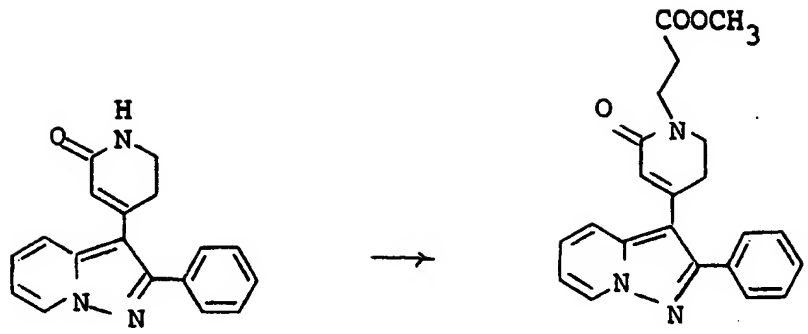
Example 33



3-[1-(2-Methoxycarbonylethyl)-5-hydroxypyrazol-3-yl]-2-phenylpyrazolo[1,5-a]pyridine was obtained according to a similar manner to that of Example 5.
mp : 194-196 °C
IR (Nujol) : 2630, 1730, 1635, 1585 cm^{-1}
NMR (DMSO-d_6, δ) : 2.49-2.53 (2H, m), 3.38 (3H, s), 5.63 (1H, s), 3.67 (2H, broad s), 7.03 (1H, td, J=7.0Hz and 1.5Hz), 7.31-7.62 (7H, m), 8.81 (1H, d, J=7.0Hz), 9.84 (1H, s)

Analysis Calcd. for $C_{20}H_{18}N_4O_3 \cdot 1/2H_2O$ (%)	
Found :	C 64.69, H 5.12, N 15.04 C 64.99, H 5.29, N 14.77

Example 34



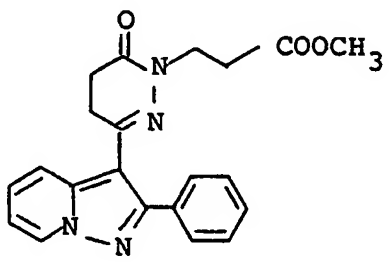
Sodium hydride (60%, 43.6 mg) was added to a mixture of 3-(2-oxo-1,2,5,6-tetrahydropyridin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine (210 mg), methyl acrylate (93.8 mg) and tetrahydrofuran (2.1 ml) under ice-cooling. The reaction mixture was stirred at room temperature for 1.5 hours. A saturated solution of sodium chloride (20 ml) was added to the reaction mixture and extracted with ethyl acetate (20 ml x 2). The combined extract was washed with a saturated solution of sodium chloride (20 ml), dried over magnesium sulfate and evaporated in vacuo. The residue was purified by column chromatography on silica gel using a mixture of chloroform and ethyl acetate (10:1) to give 3-[1-(2-methoxycarbonylethyl)-2-oxo-1,2,5,6-tetrahydropyridin-4-yl]-2-phenylpyrazolo[1,5-a]pyridine (210.7 mg) as an oil.

IR (film) : 1730, 1640, 1600, 1515 cm^{-1}

NMR ($CDCl_3$, δ) : 2.41 (2H, t, J=6.5Hz), 2.69 (2H, t, J=6.5Hz), 3.47 (2H, t, J=6.5Hz), 3.69 (3H, s), 3.72 (2H, t, J=6.5Hz), 6.20 (1H, s), 6.85 (1H, td, J=7.0Hz and 1.0Hz), 7.19-7.74 (7H, m), 8.48 (1H, d, J=7.0Hz)

MS : 375 (M^+)

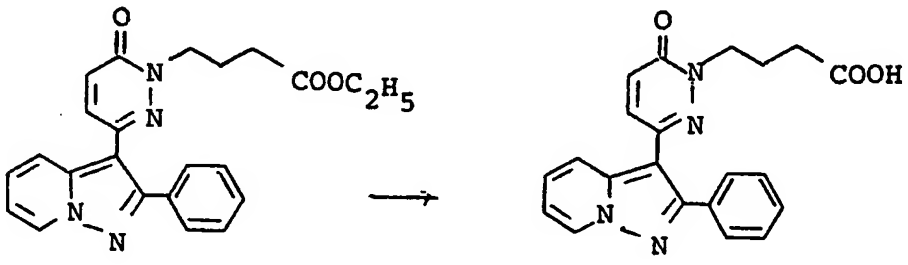
Example 35



3-[2-(2-Methoxycarbonylethyl)-3-oxo-2,3,4,5-tetrahydropyridazin-6-yl]-2-phenylpyrazolo[1,5-a]pyridine was obtained according to a similar manner to that of Example 34.

IR (film) : 1730, 1670 cm^{-1}

Example 36



A mixture of 3-[2-(3-ethoxycarbonylpropyl)-3-oxo-2,3-dihydropyridazin-6-yl]-2-phenylpyrazolo[1,5-a]-pyridine (13.7 g) and sodium hydroxide (2.73 g) in a mixture of water (8.6 ml) and methanol (96 ml) was refluxed for 2 hours and then the solvent was evaporated in vacuo. The residue was dissolved in water, and the aqueous solution was acidified with hydrochloric acid, and extracted with chloroform. The extract was dried over magnesium sulfate and the solvent was evaporated in vacuo. The residue was recrystallized from a mixture of ethanol and n-hexane to give 3-[2-(3-carboxypropyl)-3-oxo-2,3-dihydropyridazin-6-yl]-2-phenylpyrazolo[1,5-a]pyridine (9.48 g).

mp : 240-240.5° C (EtOH)

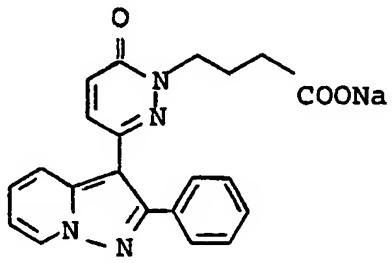
IR (Nujol) : 1710, 1635, 1560, 1530, 1500 cm^{-1}

NMR (DMSO-d_6, δ) : 1.97 (2H, g, J=7Hz), 2.26 (2H, t, J=7Hz), 3.23 (1H, broad), 4.13 (2H, t, J=7Hz), 6.77 (1H, d, J=10Hz), 7.00 (1H, td, J=7Hz and 1Hz), 7.03 (1H, d, J=10Hz), 7.90 (1H, d, J=9Hz), 7.75 (1H, d, J=7Hz)

MS (M^+) : 374

Analysis Calcd. for $C_{21}H_{18}N_4O_3$ (%)	
Found :	C 67.37, H 4.85, N 14.96 C 67.10, H 4.91, N 14.94

Example 37



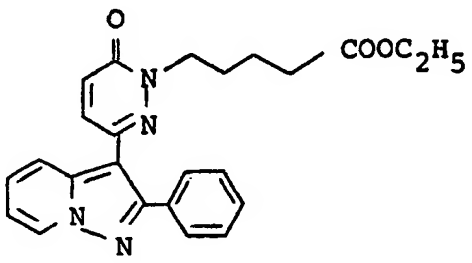
Sodium salt of 3-[2-(3-carboxypropyl)-3-oxo-2,3-dihydropyridazin-6-yl]-2-phenylpyrazolo[1,5-a]pyridine was prepared from the corresponding free compound (Example 36) according to a conventional manner.

mp : 114-116° C

IR (Nujol) : 1660, 1585 cm^{-1}

NMR (DMSO-d_6, δ) : 2.01 (4H, m), 4.15 (2H, t), 6.84 (1H, d, J=9Hz), 7.00-7.09 (2H, m), 7.39-7.62 (6H, m), 7.97 (1H, d, J=8Hz), 8.79 (1H, d, J=7Hz)

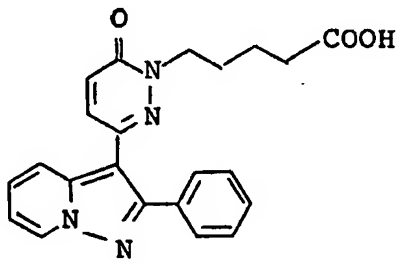
Example 38



3-[2-(4-Ethoxycarbonylbutyl)-3-oxo-2,3-dihydropyridazin-6-yl]-2-phenylpyrazolo[1,5-a]pyridine was pre-

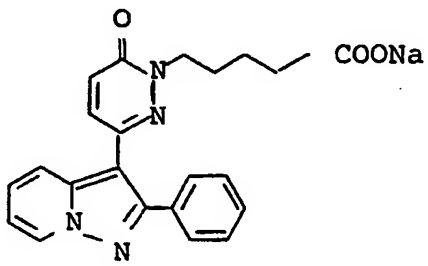
pared according to a similar manner to that of Example 26.
IR (film) : 1725, 1655, 1590 cm^{-1}
NMR ($CDCl_3$, δ) : 1.25 (3H, t, J=7Hz), 1.74-2.02 (4H, m), 2.41 (2H, t, J=7Hz), 4.13 (2H, q, J=7Hz), 4.32 (2H, t, J=7Hz), 6.87 (1H, d, J=8Hz), 7.02-7.07 (2H, m), 7.40-7.65 (6H, m), 8.05 (1H, d, J=9Hz), 8.74 (1H, d, J=7Hz)

Example 39



3-[2-(4-Carboxybutyl)-3-oxo-2,3-dihydropyridazin-6-yl]-2-phenylpyrazolo[1,5-a]pyridine was prepared according to a similar manner to that of Example 36.
mp : 182-183°C
IR (Nujol) : 1710, 1640, 1570, 1530, 1500 cm^{-1}
NMR ($CDCl_3$, δ) : 1.74-2.04 (4H, m), 2.47 (2H, t, J=6Hz), 4.31 (2H, t, J=6Hz), 6.79 (1H, d, J=10Hz), 6.91 (1H, t, J=6Hz), 7.01 (1H, d, J=10Hz), 7.26-7.63 (6H, m), 7.97 (1H, d, J=9Hz), 8.54 (1H, d, J=7Hz)

Example 40



Sodium salt of 3-[2-(4-carboxybutyl)-3-oxo-2,3-dihydropyridazin-6-yl]-2-phenylpyrazolo[1,5-a]pyridine was prepared from the corresponding free compound (Example 39) according to a conventional manner.
mp : 244-245°C
IR (Nujol) : 1660, 1650, 1570 cm^{-1}
NMR (DMSO-d_6, δ) : 1.38-1.60 (2H, m), 1.62-1.83 (2H, m), 1.92 (2H, t, J=7Hz), 4.11 (2H, t, J=7Hz), 6.85 (1H, d, J=10Hz), 7.04-7.09 (2H, m), 7.42-7.61 (6H, m), 7.95 (1H, d, J=8Hz), 8.81 (1H, d, J=7Hz)

Example 41

A mixture of 3-(3-cyano-2-oxo-1,2-dihydropyridin-5-yl)-2-phenylpyrazolo[1,5-a]pyridine (0.60 g) and 85% potassium hydroxide (0.38 g) in 67% aqueous ethanol (6 ml) was refluxed for 4 hours. After cooling, the reaction mixture was added onto ice (12 g) and acidified with 5% hydrochloric acid. Precipitates were collected and recrystallized from a mixture of N,N-dimethylformamide and water twice to give 3-(3-carboxy-2-oxo-1,2-dihydropyridin-5-yl)-2-phenylpyrazolo[1,5-a]pyridine (0.36 g).

mp : 335-336° C (dec.)

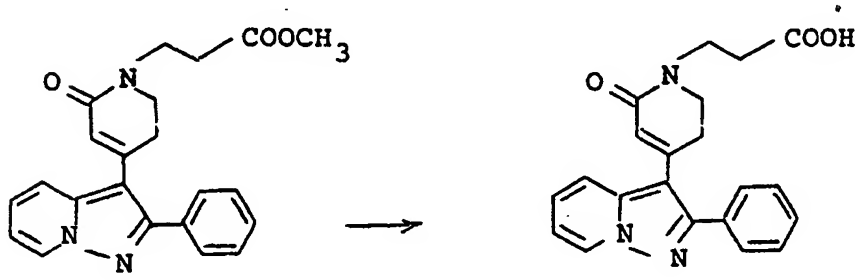
IR (Nujol) : 1700, 1630, 1585, 1535 cm^{-1}

NMR (DMSO-d_6, δ) : 6.98 (1H, t, J=7.0Hz), 7.18-7.72 (7H, m), 7.97 (1H, d, J=3.0Hz), 8.17 (1H, d, J=3.0Hz), 8.77 (1H, d, J=7.0Hz), 12.3-13.8 (2H, br)

MS : 331 (M^+), 287

Analysis Calcd. for $C_{19}H_{13}N_3O_3$ (%)	
Found :	C 68.88, H 3.95, N 12.68 C 68.58, H 3.99, N 12.63

Example 42



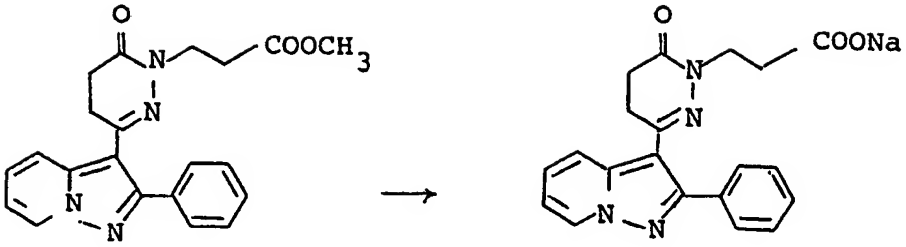
A mixture of 3-[1-(2-methoxycarbonylethyl)-2-oxo-1,2,5,6-tetrahydropyridin-4-yl]-2-phenylpyrazolo[1,5-a]-pyridine (440 mg), 1N sodium hydroxide aqueous solution (3 ml) and methanol (4 ml) was heated under reflux for 1.5 hours. Methanol was evaporated in vacuo and water (20 ml) was added to the residue. The aqueous solution was acidified with 5% hydrochloric acid and precipitates were collected by filtration, washed with water, and then with petroleum ether (5 ml). The precipitates were recrystallized from 95% ethanol to give crystals of 3-[1-(2-carboxyethyl)-2-oxo-1,2,5,6-tetrahydropyridin-4-yl]-2-phenylpyrazolo[1,5-a]pyridine (220 mg).

mp : 182-184° C

IR (Nujol) : 1735, 1640, 1585 cm^{-1}

NMR ($CDCl_3$, δ) : 2.42 (2H, t, J=6.5Hz), 2.74 (2H, t, J=6.5Hz), 3.49 (2H, t, J=6.5Hz), 3.73 (2H, t, J=6.5Hz), 6.22 (1H, s), 7.20-7.74 (8H, m), 8.49 (1H, d, J=7.0Hz)

Example 43



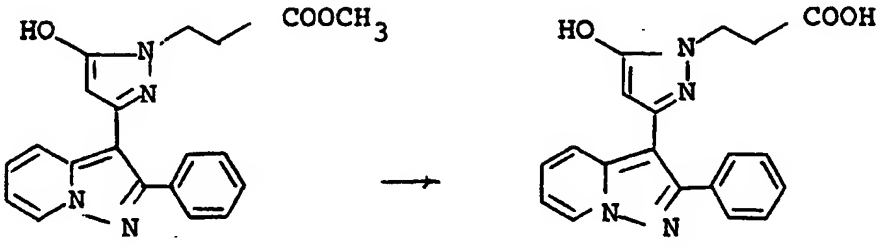
A mixture o-f 3-[2-(2-methoxycarbonylethyl)-3-oxo-2,3,4,5-tetrahydropyridazin-6-yl]-2-phenylpyrazolo-[1,5-a]pyridine (484 mg), 1N sodium hydroxide aqueous solution (2.1 ml) and methanol (5 ml) was stirred at room temperature for 1 hour. Methanol was evaporated in vacuo. To the residue, water (10 ml) was added and the solution was acidified with 5% hydrochloric acid and extracted with chloroform (20 ml x 2). The combined extracts was washed with a saturated aqueous solution of sodium chloride (20 ml), dried over magnesium sulfate and evaporated in vacuo. The residue was purified by column chromatography on silica gel using a mixture of chloroform and methanol (30:1) as an eluent to give 3-[2-(2-carboxyethyl)-3-oxo-2,3,4,5-tetrahydropyridazin-6-yl]-2-phenylpyrazolo[1,5-a]pyridine (198 mg) as an oil. This free acid was dissolved in a mixture of 1N sodium hydroxide aqueous solution (0.547 mg) and ethanol (3 ml), and the solvent was evaporated in vacuo. The residue was triturated with 95% ethanol, collected by filtration, washed with acetone and dried to give powder of sodium salt of 3-[2-(2-carboxyethyl)-3-oxo-2,3,4,5-tetrahydropyridazin-6-yl)-2-phenylpyrazolo[1,5-a]pyridine (129 mg).

IR (Nujol) : 1640, 1560, 1510 cm^{-1}

NMR (D_2O, δ) : 2.04 (4H, s), 2.25 (2H, t, J=7.5Hz), 3.71 (2H, t, J=7.5Hz), 6.71 (1H, t, J=7.0Hz), 7.08-7.23 (6H, m), 7.63 (1H, d, J=9.0Hz), 8.06 (1H, d, J=7.0Hz)

Analysis Calcd. for $C_{20}H_{17}NaN_4O_3 \cdot 3H_2O$ (%)	
Found :	C 54.79, H 5.25, N 12.99 C 55.46, H 4.71, N 12.71

Example 44



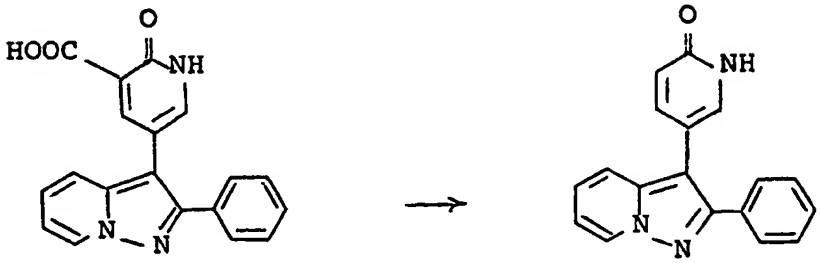
A mixture of 3-[1-(2-methoxycarbonylethyl)-5-hydroxypyrazol-3-yl]-2-phenylpyrazolo[1,5-a]pyridine (0.50 g), 1N sodium hydroxide aqueous solution (3 ml) and ethanol (5 ml) was heated under reflux for 2.5 hours. Ethanol was evaporated in vacuo. The residue was acidified with 5% hydrochloric acid and extracted with chloroform (25 ml x 2). Combined extract was washed with a saturated aqueous solution of sodium chloride (25 ml), dried over magnesium sulfate and evaporated in vacuo. The residue was purified by column chromatography on silica gel using a mixture of chloroform and methanol (30:1) as an eluent and recrystallized from ethanol to give crystal of 3-[1-(2-carboxyethyl)-5-hydroxypyrazol-3-yl]-2-phenylpyrazolo-[1,5-a]pyridine (141 mg).

mp : 211 to 213 °C

IR (Nujol) : 1705, 1610 cm^{-1}
NMR ($CDCl_3$, δ) : 2.11 (2H, broad s), 3.89 (2H, broad s), 5.83 (1H, s), 6.91 (1H, t, J=6.0Hz), 7.23-7.71 (7H, m), 8.54 (1H, d, J=6.0Hz)

Analysis Calcd. for $C_{19}H_{16}N_4O_3$ (%)	
Found :	C 65.51, H 4.63, N 16.08 C 65.10, H 4.60, N 16.16

Example 45



3-(3-Carboxy-2-oxo-1,2-dihydropyridin-5-yl)-2-phenylpyrazolo[1,5-a]pyridine (120 mg) was melted by an electric hot plate at 370° C. This was dissolved in a mixture of chloroform (26 ml) and methanol (13 ml), and silica gel (1 g) and charcoal (0.2 g) were added thereto and then this mixture was filtered. The solvent of the filtrate was removed and chromatographed on silica gel (3 g) with a mixture of chloroform, methanol and triethylamine (200:10:1). The fractions containing the object compound were combined and evaporated in vacuo and recrystallized from ethyl acetate to give 3-(2-oxo-1,2-dihydropyridin-5-yl)-2-phenylpyrazolo[1,5-a]-pyridine (30 mg).
mp : 222-224° C
IR (Nujol) : 1665, 1630 cm^{-1}
NMR (DMSO-d_6, δ) : 6.39 (1H, d, J=9.2Hz), 6.96 (1H, t, J=6.0Hz), 7.23-7.65 (9H, m), 8.73 (1H, d, J=7.0Hz), 11.75 (1H, broad s)
MS : 287 (M^+), 258, 231

Analysis Calcd. for $C_{18}H_{13}N_3O \cdot 1/3H_2O$ (%)	
Found :	C 73.70, H 4.70, N 14.34 C 73.88, H 4.53, N 14.16

Example 46

A mixture of 3-(3-chloro-1-ethoxycarbonyl-1,4-dihydropyridazin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine (1.26 g), manganese (IV) oxide (12.6 g) and chloroform (12.6 ml) was refluxed for 10 hours. After filtration, organic layer was dried over magnesium sulfate. The solvent was removed and chromatographed on silica gel (12.6 g) with a mixture of hexane and ethyl acetate as an eluent. The fractions containing the objective compound were combined and evaporated in vacuo and recrystallized from a mixture of ethyl acetate and n-hexane to give 3-(3-chloropyridazin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine (0.78 g).

mp : 208-210 °C

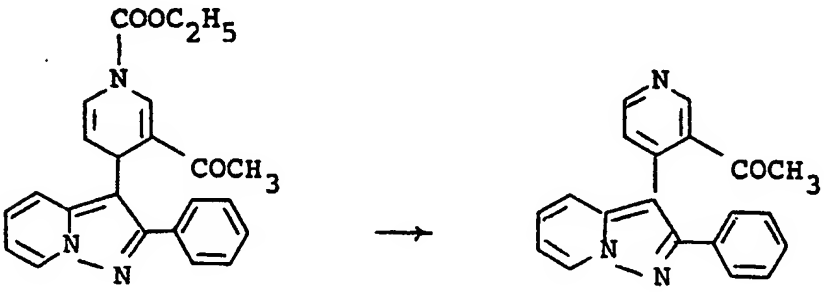
IR (Nujol) : 1635, 1570 cm^{-1}

NMR ($CDCl_3$, δ) : 6.94 (1H, dt, J=1.6Hz and 6.7Hz), 7.25-7.49 (8H, m), 8.58 (1H, ddd, J=0.96Hz, 0.96Hz, and 7.0Hz), 9.06 (1H, d, J=4.9Hz)

MS : 306 (M^+), 271, 242, 216

Analysis Calcd. for $C_{17}H_{11}ClN_4$ (%)	
Found :	C 66.56, H 3.61, N 18.26 C 66.96, H 3.63, N 18.31

Example 47



A mixture of 3-1-ethoxycarbonyl-3-acetyl-1,4-dihydropyridin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine (2.20 g), potassium tert-butoxide (3.19 g) and tert-butanol (22 ml) was refluxed for an hour and 30 minutes. The solvent was removed and the residue was extracted with methylene chloride. Combined extract was washed with water and a saturated aqueous solution of sodium chloride, and dried over magnesium sulfate. The solvent was evaporated in vacuo. The residue was chromatographed on silica gel (12 g) with a mixture of n-hexane and ethyl acetate (4:1) as an eluent. The fractions containing the object compound was combined and the solvent was evaporated in vacuo. Recrystallization from a mixture of ethyl acetate and n-hexane gave 3-(3-acetylpyridin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine (0.52 g).

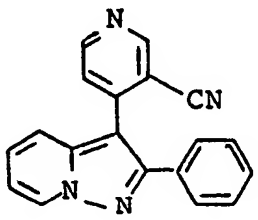
mp : 159-161 °C

IR (Nujol) : 1690, 1630 cm^{-1}

NMR ($CDCl_3$, δ) : 1.94 (3H, s), 6.83 (1H, t, J=7.5Hz), 7.17 (1H, t, J=7.5Hz), 7.20-7.53 (7H, m), 8.50 (1H, d, J=7.5Hz), 8.65 (1H, d, J=5.0Hz), 8.80 (1H, s)
MS : 313 (M^+), 298, 242, 210

Analysis Calcd. for $C_{20}H_{15}N_3O$ (%)	
Found :	C 76.66, H 4.82, N 13.41 C 76.34, H 5.48, N 13.17

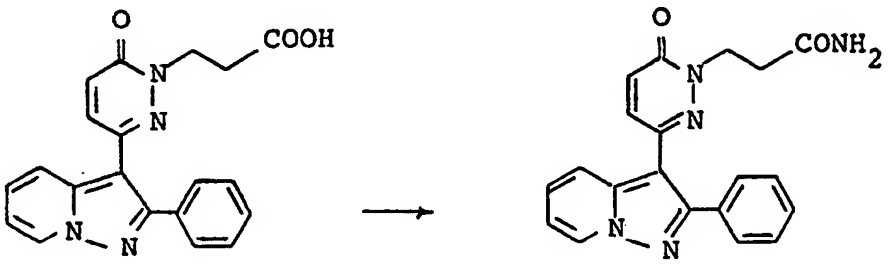
Example 48



3-(3-Cyanopyridin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine was obtained according to a similar manner to that of Example 47.
mp : 208-210 °C
IR (Nujol) : 2220, 1630, 1585 cm^{-1}
NMR ($CDCl_3$, δ) : 6.80 (1H, t, J=7.5Hz), 7.07-7.43 (8H, m), 8.43 (1H, d, J=7.5Hz), 8.53 (1H, d, J=5.0Hz), 8.77 (1H, s)
MS : 296 (M^+), 270

Analysis Calcd. for $C_{19}H_{12}N_4$ (%)	
Found :	C 77.01, H 4.08, N 18.91 C 77.30, H 4.17, N 19.02

Example 49



A mixture of 3-[2-(2-carboxyethyl)-3-oxo-2,3-dihydropyridazin-6-yl]-2-phenylpyrazolo[1,5-a]pyridine (0.36 g), methylene chloride (4 ml) and thionyl chloride (0.08 ml) was stirred for 30 minutes under room temperature, then thionyl chloride (0.08 ml) was added again and stirred for 60 minutes under room

temperature. The reaction mixture was evaporated. The residue was dissolved in acetone (3 ml). This was added slowly to aqueous ammonia solution (6 ml) stirring at room temperature. After 20 minutes, the reaction mixture was evaporated, and thereto water (3 ml) was added. Precipitates were collected by filtration and recrystallized from ethanol to give 3-[2-(2-carbamoylethyl)-3-oxo-2,3-dihydropyridazin-6-yl]-2-phenylpyrazolo[1,5-a]pyridine (0.24 g).

mp : 215-215.5° C

IR (Nujol) : 3450, 3330, 3210, 1660, 1595, 1535 cm^{-1}

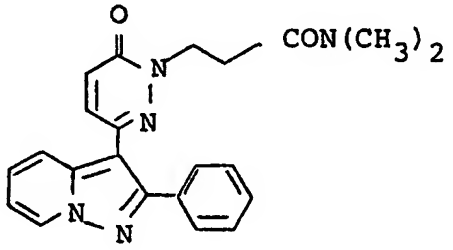
NMR ($CDCl_3$, δ) : 2.89 (2H, t, J=7Hz), 4.58 (2H, t, J=7Hz), 5.20-5.60 (1H, s), 6.00-6.50 (1H, s), 6.70 (1H, d, J=10Hz), 7.89 (1H, t, J=7Hz), 7.00 (1H, d, J=10Hz), 7.20-7.68 (6H, m), 8.03 (1H, d, J=9Hz), 8.50 (1H, d, J=7Hz)

MS (M^+) : 359

Analysis Calcd. for $C_{20}H_{17}N_5O_2$ (%)	
Found :	C 66.84, H 4.77, N 19.49 C 67.11, H 5.01, N 19.65

The following compounds (Examples 50 and 51) were obtained according to a similar manner to that of Example 49.

Example 50



3-[2-(2-N,N-Dimethylcarbamoylethyl)-3-oxo-2,3-dihydropyridazin-6-yl]-2-phenylpyrazolo[1,5-a]pyridine

mp : 144-145° C

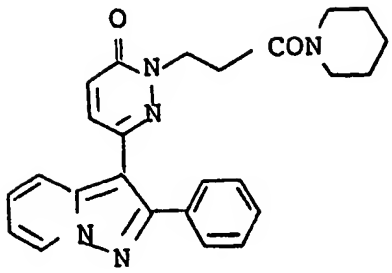
IR (Nujol) : 1665, 1640, 1590, 1530 cm^{-1}

NMR ($CDCl_3$, δ) : 2.97 (2H, t, J=8Hz), 2.98 (3H, s), 3.03 (3H, s), 4.61 (2H, t, J=8Hz), 6.75 (1H, d, J=10Hz), 6.93 (1H, td, J=6Hz and 1Hz), 7.02 (1H, d, J=10Hz), 7.26-8.64 (6H, m), 8.08 (1H, d, J=8Hz), 8.52 (1H, d, J=7Hz)

MS (M^+) : 387

Analysis Calcd. for $C_{22}H_{21}N_5O_2$	
Found :	C 68.20, H 5.46, N 18.08 C 68.60, H 5.67, N 18.04

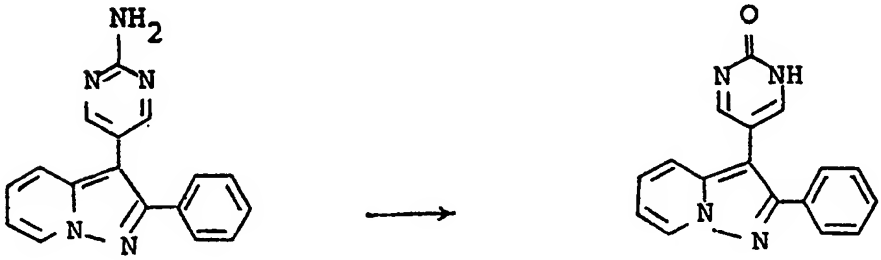
Example 51



1-[3-{6-(2-Phenylpyrazolo[1,5-a]pyridin-3-yl)-3-oxo-2,3-dihydropyridazin-2-yl}proplonyl]piperidine
mp : 65-70° C
IR (Nujol) : 1660, 1630, 1585, 1520 cm^{-1}
NMR ($CDCl_3$, δ) : 1.58-1.76 (6H, m), 2.96 (2H, t, J=8Hz), 3.49 (4H, d, J=32Hz), 4.61 (2H, t, J=8Hz), 6.75 (1H, d, J=10Hz), 6.94 (1H, td, J=7Hz and 1Hz), 7.02 (1H, d, J=10Hz), 7.26-7.63 (6H, m), 7.68 (1H, d, J=8Hz), 8.53 (1H, d, J=7Hz)
MS : 427 (M^+)

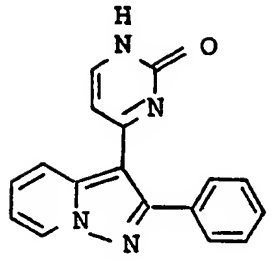
Analysis Calcd. for $C_{25}H_{25}N_5O_2$ (%)	
Found :	C 70.28, H 5.89, N 16.38 C 69.15, H 6.01, N 16.18

Example 52



To a mixture of 3-(2-aminopyrimidin-5-yl)-2-phenylpyrazolo[1,5-a]pyridine (0.70 g) and 50% sulfuric acid (5.6 ml) was gradually added aqueous solution (5.6 ml) of sodium nitrite (1.68 g) at 5 to 10° C, and the resultant mixture was stirred for 3 hours at the same temperature and then for 2 hours at room temperature. To the reaction mixture was added water (14 ml). The precipitates were collected by filtration subjected to a column chromatography on silica gel (14 g) with a mixture of chloroform and methanol (10:1) as an eluent. The fractions containing the objective compound were combined and the solvent was evaporated in vacuo to give 3-(2-oxo-1,2-dihydropyrimidin-5-yl)-2-phenylpyrazolo[1,5-a]pyridine (0.44 g).
mp : 324-326° C (dec.)
IR (Nujol) : 3200-2300, 1720, 1700, 1645, 1625 cm^{-1}
NMR (DMSO-d_6, δ) : 6.93 (1H, t, J=7.5Hz), 7.27 (1H, t, J=7.5Hz), 7.33-7.70 (6H, m), 8.15 (2H, s), 8.75 (1H, d, J=7.5Hz)
MS : 288 (M^+), 260, 246, 218

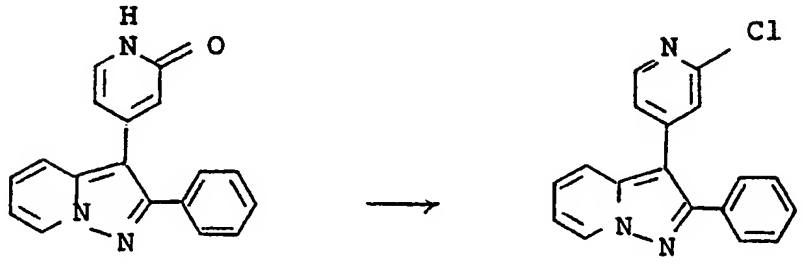
Example 53



3-(2-Oxo-1,2-dihydropyrimidin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine was obtained according to a similar manner to that of Example 52.
mp : 287-289° C
IR (Nujol) : 1640, 1610 cm^{-1}
NMR (DMSO-d_6, δ) : 5.91 (1H, d, J=6.6Hz), 7.18 (1H, t, J=6.4Hz), 7.51-7.69 (7H, m), 8.55 (1H, d, J=8.9Hz), 8.86 (1H, d, J=6.8Hz), 11.1-11.9 (1H, broad s)
MS : 287 (M^+-1), 259, 244

Analysis Calcd. for $C_{17}H_{12}N_4O \cdot 1/2H_2O$ (%)	
Found :	C 68.68, H 4.41, N 18.84 C 68.48, H 4.24, N 18.51

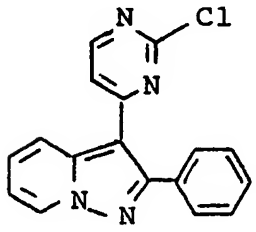
Example 54



A mixture of 3-(2-oxo-1,2-dihydropyridin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine (0.6 g) and phosphorus oxychloride (1.8 ml) was stirred for 6 hours at 70° C. After cooling, the reaction mixture was poured onto ice (30 g) and made alkaline with 24% aqueous solution of sodium hydroxide (pH = 10) and extracted with chloroform (18 ml). The combined extract was washed with water and sodium chloride aqueous solution and dried over magnesium sulfate. The solvent was removed in vacuo and the residue was chromatographed on silica gel (12 g) with chloroform as an eluent. The fractions containing the object compound were combined and evaporated in vacuo and recrystallized from a mixture of ethyl acetate and diisopropyl ether to give 3-(2-chloropyridin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine (0.21 g).
mp : 167-168° C
IR (Nujol) : 1630, 1590, 1530 cm^{-1}
NMR ($CDCl_3$, δ) : 6.91 (3H, t, J=6.8Hz), 7.15 (1H, dd, J=1.5Hz and 5.2Hz), 7.25-7.69 (6H, m), 8.32 (1H, dd, J=0.5Hz and 5.2Hz), 8.54 (1H, dd, J=1.0Hz and 6.0Hz)
MS : 305 (M^+), 270, 243

Analysis Calcd. for $C_{18}H_{12}ClN_3$ (%)	
Found :	C 70.71, H 3.96, N 13.74 C 70.51, H 3.95, N 13.62

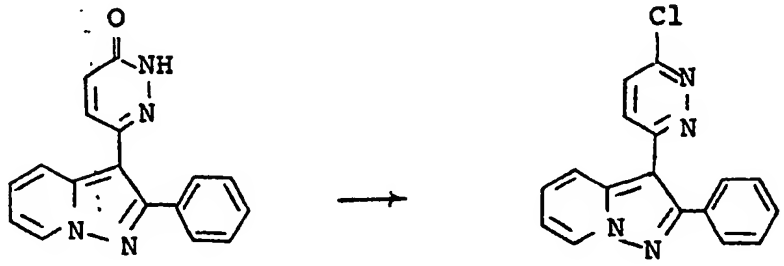
Example 55



3-(2-Chloropyrimidin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine was obtained according to a similar manner to that of Example 54.
mp : 181-182 °C
IR (Nujol) : 1630, 1570, 1530 cm^{-1}
NMR ($CDCl_3$, δ) : 6.92 (1H, d, J=5.5Hz), 7.02 (1H, dt, J=1.3Hz and 6.9Hz), 7.43-7.62 (6H, m), 8.23 (1H, d, J=5.4Hz), 8.55 (1H, d, J=6.9Hz), 8.64 (1H, d, J=9.0Hz)
MS : 306 (M^+), 271, 244, 217

Analysis Calcd. for $C_{17}H_{11}ClN_4$ (%)	
Found :	C 66.56, H 3.61, N 18.26 C 66.30, H 3.52, N 18.59

Example 56

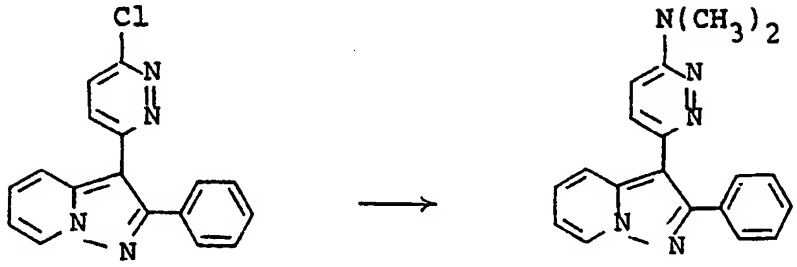


A mixture.of 3-(3-oxo-2,3-dihydropyridazin-6-yl)-2-phenylpyrazolo[1,5-a]pyridine (2.91 g) and phosphorus oxychloride (10 ml) was heated under reflux for 1 hour. Phosphorus oxychloride was evaporated in vacuo. The residue was neutralized by saturated aqueous solution of sodium hydrogen carbonate and extracted with chloroform (30 ml x 3). The combined extract was washed with a saturated aqueous solution of sodium chloride (20 ml) and dried over magnesium sulfate. The solvent was evaporated in vacuo and the residue was triturated with ethanol, collected by filtration, washed with ethanol and dried to give crystals of 3-(3-chloropyridazin-6-yl)-2- phenylpyrazolo[1,5-a]pyridine (2.42 g).

mp : 208-211 °C
IR (Nujol) : 1630, 1575, 1530 cm^{-1}
NMR (DMSO-d_6, δ) : 7.14 (1H, td, J=7.0Hz and 1.0Hz), 7.36 (1H, d, J=9.0Hz), 7.47-7.60 (6H, m), 7.78 (1H, d, J=9.0Hz), 8.16 (1H, d, J=9.0Hz), 8.87 (1H, d, J=7.0Hz)

Analysis Calcd. for $C_{17}H_{11}ClN_4$ (%)	
Found :	C 63.65, H 3.53, N 17.22 C 63.14, H 3.48, N 17.29

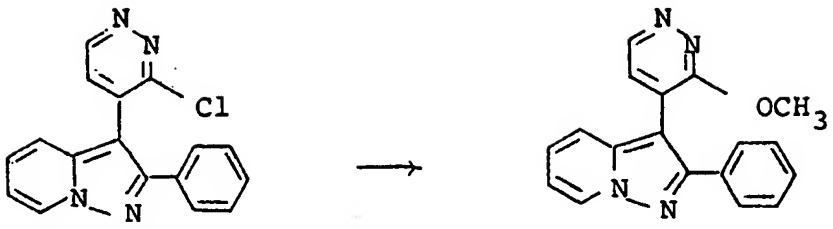
Example 57



A mixture of 3-[3-chloropyridazin-6-yl)-2-phenylpyrazolo[1,5-a]pyridine (1.00 g) and a solution of dimethylamine in methanol (30 ml) was heated under reflux for 8.5 hours. Methanol was evaporated in vacuo and the residue was dissolved in chloroform (50 ml). The chloroform solution was extracted with 10% hydrochloric acid (50 ml x 2). The aqueous layer was neutralized with potassium carbonate and extracted with chloroform (30 ml x 2). The combined extract was washed with a saturated aqueous solution of sodium chloride (30 ml), dried over magnesium sulfate and evaporated in vacuo. The residue was recrystallized from ethanol to give crystal of 3-(3-N,N-dimethylaminopyridazin-6-yl)-2-phenylpyrazolo[1,5-a]pyridine (421 mg).
mp : 190-194 °C
IR (Nujol) : 1630, 1605, 1550, 1530 cm^{-1}
NMR (DMSO-d_6, δ) : 3.13 (6H, s), 6.99-7.07 (3H, m), 7.31-7.59 (6H, m), 7.96 (1H, d, J=9.0Hz), 8.79 (1H, d, J=6.0Hz)

Analysis Calcd. for $C_{19}H_{17}N_5$ (%)	
Found :	C 72.36, H 5.43, N 22.21 C 72.50, H 5.33, N 22.16

Example 58



To a 28% methanolic solution of sodium methoxide (3 ml) was added 3-(3-chloropyridazin-4-yl)-2-phenylpyrazolo[1.5-a]pyridine (0.61 g). The mixture was refluxed for an hour and evaporated in vacuo. The residue was dissolved in chloroform (20 ml). The chloroform solution was washed with water (5 ml) and a saturated aqueous solution of sodium chloride (5 ml) and dried over magnesium sulfate. The solvent was removed and chromatographed on silica gel (10 g) with n-hexane-ethyl acetate as an eluent. The fractions containing the object compound were combined, evaporated in vacuo, and then recrystallized from a mixture of ethyl acetate and n-hexane to give 3-(3-methoxypyridazin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine (0.30 g).

mp : 180-182°C

IR (Nujol) : 1630, 1580, 1510 cm^{-1}

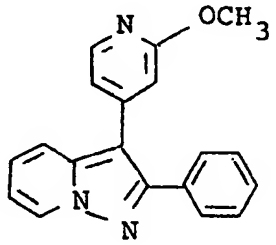
NMR ($CDCl_3$, δ) : 3.97 (3H, s), 6.89 (1H, dt, J = 1.4Hz and 6.4Hz), 7.20-7.52 (8H, m), 8.55 (1H, d, J = 6.9Hz), 8.79 (1H, d, J = 4.8Hz)

MS : 302 (M^+), 279

Analysis Calcd. for $C_{18}H_{14}N_4O$ (%)	
Found :	C 71.51, H 4.67, N 18.53 C 71.45, H 4.68, N 18.63

The following compounds (Examples 59 and 60) were obtained according to a similar manner to that of Example 58.

Example 5



3-(2-Methoxypyridin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine

mp : 130-132°C

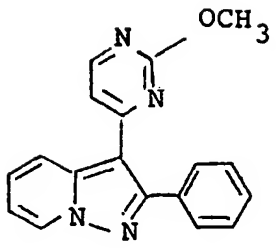
IR (Nujol) : 1600, 1530 cm^{-1}

NMR ($CDCl_3$, δ) : 3.96 (3H, s), 6.80-6.88 (2H, m), 7.19 (1H, dt, J = 1.0Hz and 6.8Hz), 7.36-7.39 (3H, m), 7.57-7.67 (3H, m), 8.12 (1H, dd, J = 1.2Hz and 4.9Hz), 8.52 (1H, dd, J = 0.9Hz and 7.0Hz)

MS : 301 (M^+), 270

Analysis Calcd. for $C_{19}H_{15}N_3O$ (%)	
Found :	C 75.73, H 5.02, N 13.94 C 75.72, H 4.97, N 13.78

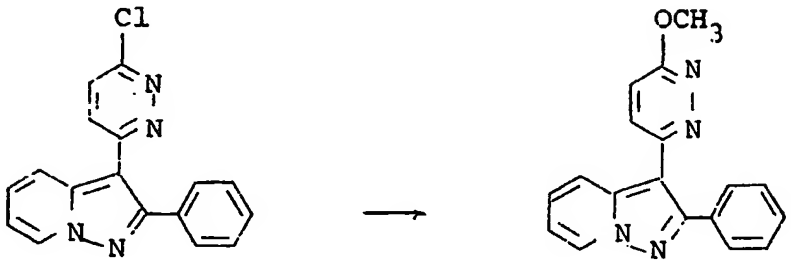
Example 60



3-(2-Methoxypyrimidin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine
mp : 156.5-157 °C
IR (Nujol) : 1620, 1570 cm^{-1}
NMR ($CDCl_3$, δ) : 4.08 (3H, s), 6.70 (1H, d, J=5.4Hz), 6.96 (1H, dt, J=1.4Hz and 6.8Hz), 7.34-7.64 (6H, m), 8.22 (1H, d, J=5.4Hz), 8.55 (2H, m)
MS : 301 (M^+-1), 271, 243

Analysis Calcd. for $C_{18}H_{14}N_4O$ (%)	
Found :	C 71.51, H 4.67, N 18.53 C 71.44, H 4.68, N 18.47

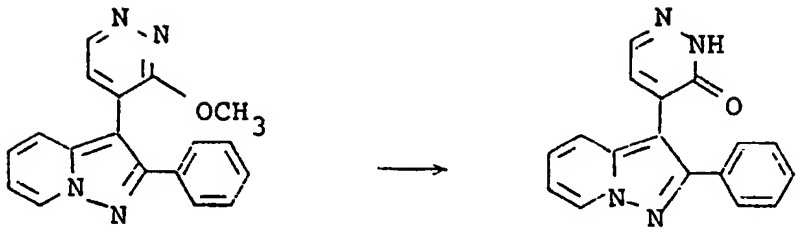
Example 61



A solution of sodium methoxide in methanol (28%, 411 mg) was added to a mixture of 3-(3-chloropyridazin-6-yl)-2-phenylpyrazolo[1,5-a]pyridine (436 mg) and methanol (4 ml) at room temperature. The reaction mixture was heated under reflux for 3 hours. After evaporating the solvent in vacuo, a saturated aqueous solution of sodium chloride (20 ml) was added to the residue and extracted with chloroform (20 ml x 3). The combined extract was washed with a saturated aqueous solution of sodium chloride (20 ml), dried over magnesium sulfate and evaporated in vacuo. The residue was purified by column chromatography on silica gel (10 g) using chloroform as an eluent and recrystallized from 95% EtOH to give 3-(3-methoxypyridazin-6-yl)-2-phenylpyrazolo[1,5-a]pyridine (165 mg).
mp : 203-205 °C
IR (Nujol) : 1625, 1600 cm^{-1}
NMR ($CDCl_3$, δ) : 4.18 (3H, s), 6.78 (1H, d, J=9.0Hz), 6.90 (1H, td, J=8.0Hz and 2.0Hz), 7.15 (1H, d, J=9.0Hz), 7.25-7.62 (6H, m), 8.36 (1H, dd, J=9.0Hz and 1.0Hz), 8.53 (1H, dd, J=7.0Hz and 1.0Hz)

Analysis Calcd. for $C_{18}H_{14}N_4O$ (%)	
Found :	C 71.51, H 4.67, N 18.53 C 71.13, H 4.65, N 18.48

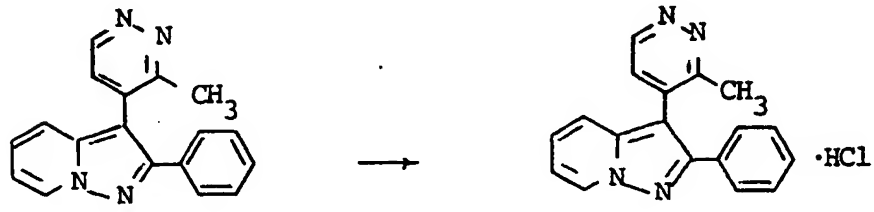
Example 62



A concentrated hydrochloric acid (5 ml) was added to 3-(3-methoxypyridazin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine (0.50 g) and refluxed for 2 hours and 30 minutes. After cooling, to the reaction mixture was added water (10 ml). The precipitates were collected by filtration to give 3-(3-oxo-2,3-dihydropyridazin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine (0.41 g).
IR (Nujol) : 1640, 1600, 1530 cm^{-1}
NMR (DMSO-d_6, δ) : 7.01 (1H, t, J=6.8Hz), 7.22 (1H, d, J=4.1Hz), 7.28-7.61 (7H, m), 7.84 (1H, d, J=4.1Hz), 8.78 (1H, d, J=6.9Hz), 13.18 (1H, broad s)
MS : 288 (M^+), 261, 231

Analysis Calcd. for $C_{17}H_{12}N_4O$ (%)	
Found :	C 70.82, H 4.20, N 19.43 C 70.87, H 4.15, N 19.88

Example 63

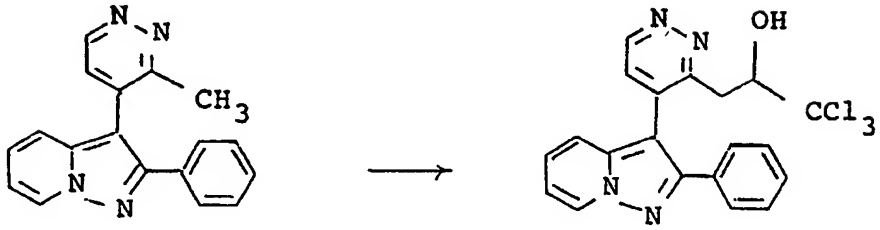


To a ethanol (21 ml) solution of 3-(3-methylpyridazin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine (0.42 g) was added 20 W/V % ethanolic hydrogen chloride solution at room temperature, and stirred for an hour. The precipitates were collected by filtration to give 3-(3-methylpyridazin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine hydrochloride (0.23 g).
mp : 197-201 °C (dec.)
IR (Nujol) : 2700-2150, 2080-1980, 1625, 1605 cm^{-1}
NMR (DMSO-d_6/D_2O, δ) : 2.30 (3H, s), 7.10 (1H, t, J=7.5Hz), 7.37 (1H, t, J=7.5Hz), 7.40-7.67 (6H, m), 8.10

(1H, d, J=5.0Hz), 8.82 (1H, d, J=7.5Hz), 9.30 (1H, d, J=5.0Hz)
MS : 286 (M^+-HCl), 257, 242, 218

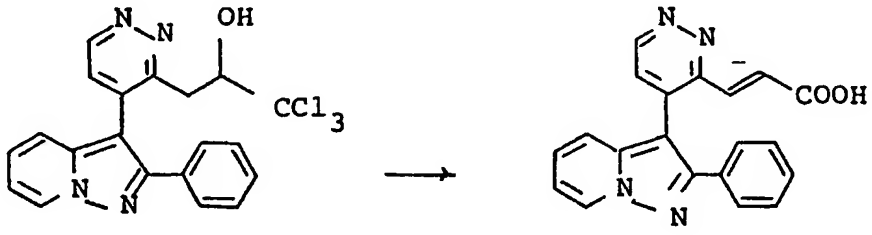
Analysis Calcd. for $C_{18}H_{14}N_4 \cdot HCl$ (%)	
Found :	C 66.98, H 4.68, N 17.36 C 66.26, H 5.09, N 16.82

Example 64



A mixture of 3-(3-methylpyridazin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine (0.40 g), chloral hydrate (0.70 g) and pyridine (4 ml) was stirred for 20 hours at 90-100° C. After cooling, to the reaction mixture was added methylene chloride (4 ml) and water (4 ml) at room temperature, and stirred for 3 hours. The precipitates were collected by filtration to give 3-[3-(2-hydroxy-3,3,3-trichloropropyl)pyridazin-4-yl]-2-phenylpyrazolo[1,5-a]pyridine (0.26 g).
mp : 206-207° C
IR (Nujol) : 3400-2900, 1625 cm^{-1}
NMR ($CDCl_3$, δ) : 2.70-3.60 (2H, m), 4.50-5.30 (1H, m), 6.80 (1H, t, J=7.5Hz), 7.13-7.40 (8H, m), 7.45 (1H, d, J=7.5Hz), 9.02 (1H, d, J=6.0Hz)
MS : 434 (M^+), 397, 361, 326, 286

Example 65



To an ethanol (12 ml) solution of 3-[3-(2-hydroxy-3,3,3-trichloropropyl)pyridazin-4-yl]-2-phenylpyrazolo-[1,5-a]pyridine (1.20 g) was added 24% aqueous sodium hydroxide solution (4.8 ml), and refluxed for 5 hours. The reaction mixture was evaporated in vacuo and added 10% hydrochloric acid (12 ml). The precipitates were collected by filtration to give 3-[3-{(E)-2-carboxyvinyl}pyridazin-4-yl]-2-phenylpyrazolo[1,5-a]pyridine (0.64 g).
mp : 227-229° C (dec.)
IR (Nujol) : 3100, 2550, 1930, 1700, 1630 cm^{-1}
MS : 342 (M^+), 297, 257, 195
NMR (DMSO-d_6, δ) : 6.77 (1H, d, J=16.5Hz), 7.06 (1H, t, J=7.5Hz), 7.22 (1H, d, J=16.5Hz), 7.34-7.55 (7H,

m), 7.70 (1H, d, J=6.0Hz), 8.33 (1H, d, J=8.5Hz), 9.25 (1H, d, J=6.0Hz), 11.8-12.8 (1H, broad s)

The following compounds (Examples 66 to 74) were prepared according to similar manners to those of Example 1 and Example 2.

Example 66

3-(3-Chloropyridazin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine

mp : 208-210 °C

IR (Nujol) : 1635, 1570 cm^{-1}

Example 67

3-(3-Acetylpyridin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine

mp : 159-161 °C

IR (Nujol) : 1690, 1630 cm^{-1}

Example 68

3-(3-Cyanopyridin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine

mp : 208-210 °C

IR (Nujol) : 2220, 1630, 1585 cm^{-1}

Example 69

3-(2-Chloropyridin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine

mp : 167-168 °C

IR (Nujol) : 1630, 1590, 1530 cm^{-1}

Example 70

3-(3-Chloropyridazin-6-yl)-2-phenylpyrazolo[1,5-a]pyridine

mp : 208-211 °C

IR (Nujol) : 1630, 1575, 1530 cm^{-1}

Example 71

3-(3-Methoxypyridazin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine

mp : 180-182 °C

IR (Nujol) : 1630, 1580, 1510 cm^{-1}

Example 72

3-(2-Methoxypyridin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine

Example 73

3-(3-Methoxypyridazin-6-yl)-2-phenylpyrazolo[1,5-a]pyridine

mp : 203-205 °C

IR (Nujol) : 1625, 1600 cm^{-1}

Example 74

3-(3-Methylpyridazin-4-yl)-2-phenylpyrazolo[1,5-a]pyridine hydrochloride

mp : 197-201 °C (dec.)

IR (Nujol) : 2700-2150, 2080-1980, 1625, 1605 cm^{-1}

The following compounds (Example 75 to 89) were prepared according to a similar manner to that of Example 5.

Example 75

3-[2-(2-Carboxyethyl)-3-oxo-2,3-dihydropyridazin-6-yl]-2-phenylpyrazolo[1,5-a]pyridine

mp : 155.5-156 °C

IR (Nujol) : 1835, 1640, 1570, 1520, 1490 cm^{-1}

Example 76

3-(1-Methylpyrazol-4-yl)-2-phenylpyrazolo[1,5-a]pyridine

mp : 100-103 °C

IR (Nujol) : 1630 cm^{-1}

Example 77

3-[2-(3-Carboxypropyl)-3-oxo-2,3-dihydropyridazin-6-yl]-2-phenylpyrazolo[1,5-a]pyridine

mp : 240-240.5 °C

IR (Nujol) : 1710, 1635, 1560, 1530, 1500 cm^{-1}

Example 78

3-[2-(4-Carboxybutyl)-3-oxo-2,3-dihydropyridazin-6-yl]-2-phenylpyrazolo[1,5-a]pyridine

mp : 182-183 °C

IR (Nujol) : 1710, 1640, 1570, 1530, 1500 cm^{-1}

Example 79

3-[1-(2-Carboxyethyl)-2-oxo-1,2,5,6-tetrahydropyridin-4-yl]-2-phenylpyrazolo[1,5-a]pyridine

mp : 182-184 °C

IR (Nujol) : 1735, 1640, 1585 cm^{-1}

Example 80

Sodium salt of 3-[2-(2-carboxyethyl)-3-oxo-2,3,4,5-tetrahydropyridazin-6-yl]-2-phenylpyrazolo[1,5-a]pyridine

IR (Nujol) : 1640, 1560, 1510 cm^{-1}

Example 81

3-[1-(2-Carboxyethyl)-5-hydroxypyrazol-3-yl]-2-phenylpyrazolo[1,5-a]pyridine

mp : 211-213 °C

IR (Nujol) : 1705, 1610 cm^{-1}

Example 82

3-[2-(2-Carbamoylethyl)-3-oxo-2,3-dihydropyridazin-6-yl]-2-phenylpyrazolo[1,5-a]pyridine

mp : 215-215.5 °C

IR (Nujol) : 3450, 3330, 3210, 1660, 1595, 1535 cm^{-1}

Example 83

3-[2-(2-N,N-Dimethylcarbamoylethyl)-3-oxo-2,3-dihydropyridazin-6-yl]-2-phenylpyrazolo[1,5-a]pyridine

mp : 144-145 °C

IR (Nujol) : 1665, 1640, 1590, 1530 cm^{-1}

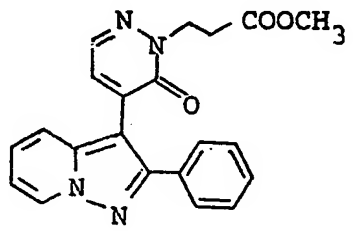
Example 84

1-[3-{6-(2-Phenylpyrazolo[1,5-a]pyridin-3-yl)-3-oxo-2,3-dihydropyridazin-2-yl}propionyl]piperidine

mp : 65-70 °C

IR (Nujol) : 1660, 1630, 1585, 1520 cm^{-1}

Example 85



3-[2-(2-Methoxycarbonylethyl)-3-oxo-2,3-dihydropyridazin-4-yl]-2-phenylpyrazolo[1,5-a]pyridine

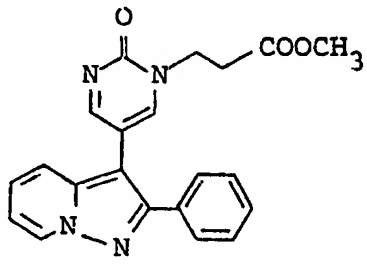
mp : 136-138 °C

IR (Nujol) : 1730, 1640, 1600 cm^{-1}

NMR ($CDCl_3$, δ) : 2.92 (2H, t, J = 6.0Hz), 3.72 (3H, s), 4.57 (2H, t, J = 6.0Hz), 6.82 (1H, t, J = 7.0Hz), 6.91 (1H, d, J = 4.5Hz), 7.1-7.7 (8H, m), 8.55 (1H, d, J = 7.0Hz)

MS : 374 (M^+), 315, 287

Example 86



3-[1-(2-Methoxycarbonylethyl)-2-oxo-1,2- dihydropyrimidin-5-yl]-2-phenylpyrazolo[1,5-a]pyridine

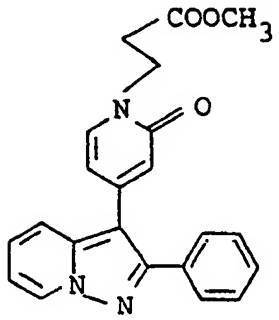
mp : 115-118 °C

IR (Nujol) : 1730, 1660 cm^{-1}

NMR ($CDCl_3$, δ) : 2.97 (2H, t, J = 6.0Hz), 3.66 (3H, s), 4.16 (2H, t, J = 6.0Hz), 6.82 (1H, t, J = 7.5Hz), 7.21 (1H, t, J = 7.5Hz), 7.33-7.73 (6H, m), 7.91 (1H, d, J = 4.0Hz), 8.49 (1H, d, J = 4.0Hz), 8.52 (1H, s)

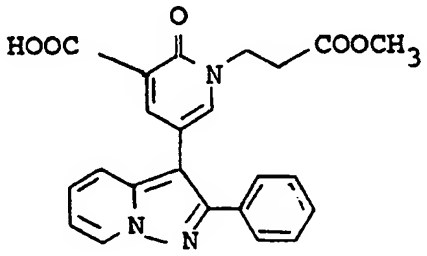
MS : 374 (M^+), 332, 288, 272

Example 87



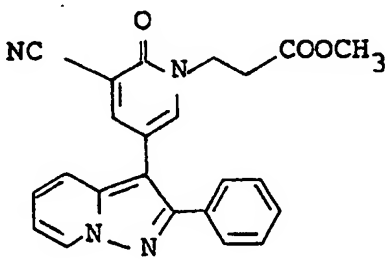
3-[1-(2-Methoxycarbonylethyl)-2-oxo-1,2-dihydropyridin-4-yl]-2-phenylpyrazolo[1,5-a]pyridine
mp : 173-174°C
IR (Nujol) : 1740, 1660, 1590 cm^{-1}
NMR ($CDCl_3$, δ) : 2.91 (2H, t, J=6.3Hz), 3.69 (3H, s), 4.21 (2H, t, J=6.3Hz), 5.98 (1H, dd, J=1.9Hz and 7.1Hz), 6.72 (1H, d, J=1.8Hz), 6.86 (1H, dt, J=14Hz and 6.9Hz), 7.2-7.4 (1H, m, J=7Hz), 7.6-7.7 (2H, m), 7.74 (1H, d, J=9.0Hz), 8.51 (1H, d, J=7.0Hz)
MS : 373 (M^+), 314, 286

Example 88



3-[1-(2-Methoxycarbonylethyl)-3-carboxy-2-oxo-1,2-dihydropyridin-5-yl]-2-phenylpyrazolo[1,5-a]pyridine
mp : 185-186°C
IR (Nujol) : 1725, 1630, 1560 cm^{-1}
NMR ($CDCl_3$, δ) : 2.92 (2H, t, J=6.0Hz), 3.68 (3H, s), 4.31 (2H, t, J=6.0Hz), 6.89 (1H, t, J=7.5Hz), 7.1-7.7 (7H, m), 7.80 (1H, d, J=3.0Hz), 8.50 (1H, d, J=7.5Hz), 8.57 (1H, d, J=3.0Hz)
MS : 373, 314, 287

Example 89

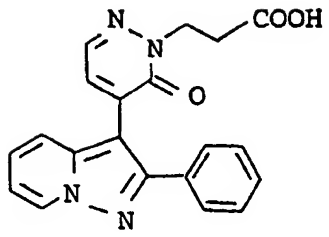


3-[1-(2-Methoxycarbonylethyl)-3-cyano-2-oxo-1,2-dihydropyridin-5-yl]-2-phenylpyrazolo[1,5-a]pyridine
mp : 155-157°C
IR (Nujol) : 2225, 1725, 1660, 1620 cm^{-1}
NMR ($CDCl_3$, δ) : 2.90 (2H, t, J=6.0Hz), 2.63 (3H, s), 4.20 (2H, t, J=6.0Hz), 6.81 (1H, t, J=7.5Hz), 7.20 (1H, t, J=7.5Hz), 7.4-7.7 (7H, m), 7.78 (1H, d, J=3.0Hz), 7.49 (1H, d, J=7.5Hz)
MS : 398 (M^+), 312

The following compounds (Examples 90 to 92) were obtained according to a similar manner to that of

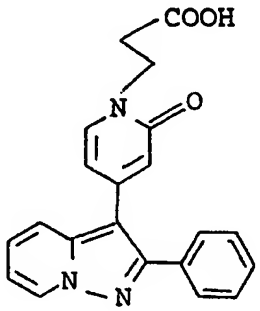
Example 6.

Example 90



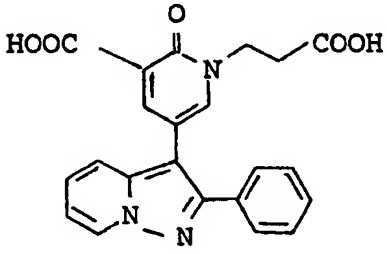
3-[2-(2-Carboxyethyl)-3-oxo-2,3-dihydropyridazin-4-yl]-2-phenylpyrazolo[1,5-a]pyridine
mp : 150-152 °C
IR (Nujol) : 1710, 1630, 1590 cm^{-1}
NMR ($CDCl_3$, δ) : 2.97 (2H, t, J=7.0Hz), 4.58 (2H, t, J=7.0Hz), 6.87 (1H, dt, J=1.3Hz and 6.9Hz), 6.95 (1H, d, J=4.2Hz), 7.2-7.7 (8H, m), 8.53 (1H, d, J=6.9Hz)
MS : 360 (M^+), 288

Example 91



3-[1-(2-Carboxyethyl)-2-oxo-1,2-dihydropyridin-4-yl]-2-phenylpyrazolo[1,5-a]pyridine
mp : 238-241 °C
IR (Nujol) : 1700, 1640 cm^{-1}
IR (DMSO-d_6, δ) : 2.70 (2H, t, J=7.5Hz), 4.06 (2H, t, J=7.5Hz), 6.04 (1H, dd, J=1.9Hz and 7.0Hz), 6.37 (1H, d, J=1.9Hz), 7.04 (1H, dt, J=1.3Hz and 6.9Hz), 7.3-7.7 (7H, m), 7.74 (1H, d, J=8.8Hz), 8.80 (1H, d, J=6.9Hz), 12.2-12.6 (1H, broad)
MS : 358 (M^+), 314, 286

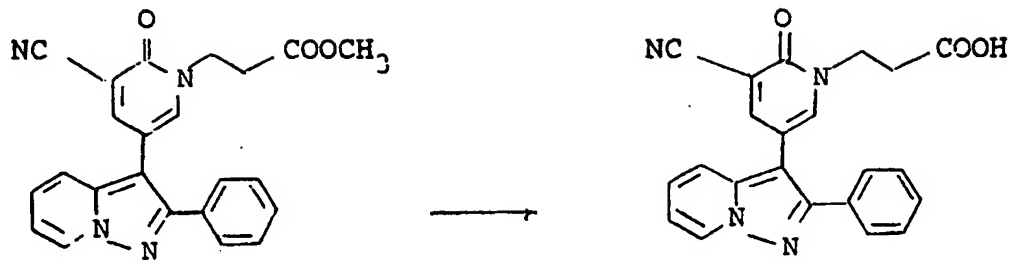
Example 92



3-[1-(2-Carboxyethyl)-3-carboxy-2-oxo-1,2-dihydropyridin-5-yl]-2-phenylpyrazolo[1,5-a]pyridine
mp : 209-211 °C
IR (Nujol) : 1730, 1690, 1630 cm^{-1}
NMR (DMSO-d_6, δ) : 2.83 (2H, t, J=6.0Hz), 4.35 (2H, t, J=6.0Hz), 6.98 (1H, t, J=7.5Hz), 7.2-7.8 (7H, m), 8.03 (1H, d, J=3.0Hz), 8.44 (1H, d, J=3.0Hz), 8.75 (1H, dd, J=7.5Hz)

MS : 403 (M^+), 331, 287

Example 93



A mixture of 3-[1-(2-methoxycarbonylethyl)-3-cyano-2-oxo-1,2-dihydropyridin-5-yl]-2-phenylpyrazolo[1,5-a]pyridine (0.46 g) and potassium carbonate (0.92 g) in 80% aqueous ethanol (4.6 ml) was stirred for 6 hours at 80° C. The mixture was acidified with 5% hydrochloric acid (pH ≒ 2). The resultant precipitates were collected by filtration, washed with water (10 ml), and subjected to a column chromatography on silica gel (10 g) with a mixture of chloroform, methanol and acetic acid (40:4:1). The fractions containing the object compound were combined and evaporated in vacuo to give 3-[1-(2-carboxyethyl)-3-cyano-2-oxo-1,2-dihydropyridin-5-yl]-2-phenylpyrazolo[1,5-a]pyridine (0.40 g).

mp : 196-200° C

IR (Nujol) : 3400, 2230, 1720, 1660, 1600 cm^{-1}

NMR (DMSO-d_6, δ, 6) : 2.69 (2H, t, J=6.0Hz), 4.18 (2H, t, J=6.0Hz), 6.99 (1H, t, J=7.8Hz), 7.31 (1H, t, J=7.8Hz), 7.4-7.7 (5H, m), 7.77 (1H, d, J=9.0Hz), 7.92 (1H, d, J=3.0Hz), 8.30 (1H, d, J=3.0Hz), 8.76 (1H, d, J=7.8Hz)

MS : 384 (M^+), 312

The following compounds (Example 94 to 97) were obtained according to a similar manner to that of Example 5.

Example 94

3-[2-(2-Carboxyethyl)-3-oxo-2,3-dihydropyridazin-4-yl]-2-phenylpyrazolo[1,5-a]pyridine

IR (Nujol) : 1710, 1630, 1590 cm^{-1}

Example 95

3-[1-(2-Carboxyethyl)-2-oxo-1,2-dihydropyridin-4-yl]-2-phenylpyrazolo[1,5-a]pyridine

IR (Nujol) : 1700, 1640 cm^{-1}

Example 96

3-[1-(2-Carboxyethyl)-3-carboxy-2-oxo-1,2-dihydropyridin-5-yl]-2-phenylpyrazolo[1,5-a]pyridine

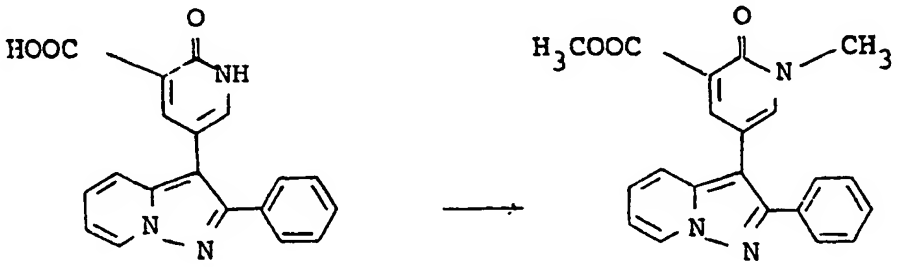
IR (Nujol) : 1730, 1690, 1630 cm^{-1}

Example 97

3-[1-(2-Carboxyethyl)-3-cyano-2-oxo-1,2-dihydropyridin-5-yl]-2-phenylpyrazolo[1,5-a]pyridine

IR (Nujol) : 3400, 2230, 1720, 1660, 1600 cm^{-1}

Example 98



To a mixture of 3-(3-carboxy-2-oxo-1,2-dihydropyridin-5-yl)-2-phenylpyrazolo[1,5-a]pyridine (0.92 g) and

potassium hydroxide powder (0.54 g) in N,N-dimethylformamide (9 ml) was added 93% methyl iodide (0.64 ml) under ice-cooling (0-5 °C) The mixture was stirred for 3 hours under ice-cooling, and then at room temperature for 1 hour and diluted with water. The resultant precipitates were filtered off and the filtrate was acidified with 5% hydrochloric acid and extracted with ethyl acetate (20 ml). The extract was washed with water (5 ml) and sodium chloride aqueous solution (5 ml), then dried over magnesium sulfate. The solvent was removed and the residue was chromatographed on silica gel (12 g) with a mixture of chloroform and methanol (100:1) as an eluent. The fractions containing the object compound were combined and evaporated in vacuo to give 3-(1-methyl-3-methoxycarbonyl-2-oxo-1,2-dihydropyridin-5-yl)-2-phenylpyrazolo[1,5-a]pyridine (0.34 g).

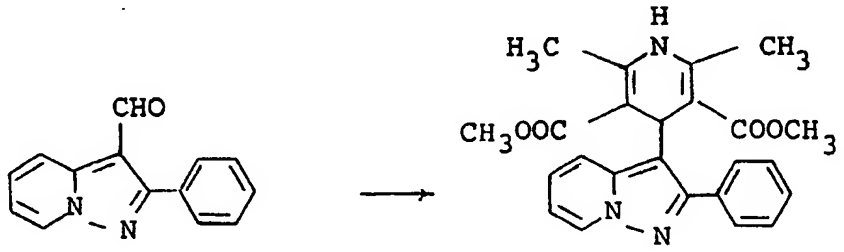
mp : 268-270 °C

IR (Nujol) : 1690, 1670, 1620 cm^{-1}

NMR ($CDCl_3$, δ) : 3.54 (3H, s), 3.86 (3H, s), 6.82 (1H, t, J=2.5Hz), 7.18 (1H, t, J=7.5Hz), 7.2-7.8 (9H, m), 8.18 (1H, s), 8.50 (1H, d, J=7.5Hz)

MS : 359 (M^+)

Example 99



A mixture of 2-phenylpyrazolo[1,5-a]pyridine-3-carbaldehyde (1.00 g), methyl acetoacetate (1.10 g), and 14% methanolic ammonia (18 ml) in a mixture of methanol (20 ml) and chloroform (10 ml) was stirred for 246 hours at room temperature. The solvent was removed in vacuo and the residue was dissolved in methylene chloride (30 ml). The solution was washed with water (10 ml) and sodium chloride aqueous solution (10 ml), dried over magnesium sulfate and evaporated in vacuo. The residue was chromatographed on silica gel (15 g) with a mixture of n-hexane and ethyl acetate (2:1). The fractions containing the object compound were combined and evaporated in vacuo to give 3-[2,6-dimethyl-3,5-bis(methoxycarbonyl)-1,4-dihydropyridin-4-yl]-2-phenylpyrazolo[1,5-a]pyridine. This compound was purified from a mixture of ethyl acetate and n-hexane.

mp : 183-186 °C

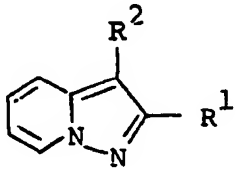
IR (Nujol) : 3330, 3250, 3120, 1690 cm^{-1}

NMR ($CDCl_3$, δ) : 2.13 (6H, s), 3.37 (6H, s), 5.19 (1H, broad), 5.51 (1H, s), 6.69 (1H, t, J=6.8Hz), 7.06 (1H, t, J=6.8Hz), 7.3-7.7 (6H, m), 8.36 (1H, d, J=6.8Hz)

MS : 417 (M^+), 358

Claims

1. A pyrazolopyridine compound of the formula :



wherein
R^1 is aryl, and
R^2 is unsaturated heterocyclic group which may have one or more suitable substituent(s),
and a pharmaceutically acceptable salt thereof.

2. A compound of claim 1, wherein
R^2 is unsaturated 3 to 8-membered heteromonocyclic group containing 1 to 4 nitrogen atom(s) or unsaturated condensed heterocyclic group containing 1 to 2 sulfur atom(s) and 1 to 3 nitrogen atom(s), each of which may have one or more suitable substituent(s).

3. A compound of claim 2, wherein
R^1 is phenyl, and
R^2 is pyridazinyl, dihydropyridazinyl, tetrahydropyridazinyl, pyrimidinyl, dihydropyrimidinyl, pyridyl, dihydropyridyl, tetrahydropyridyl, pyrazolyl or imidazothiadiazolyl, each of which may have one or more suitable substituent(s) selected from a group consisting of lower alkyl which may have one or more suitable substituent(s), carboxy(lower)alkenyl, amino, di(lower)alkylamino, halogen, lower alkoxy, oxo, hydroxy, cyano and an acyl group.

4. A compound of claim 3, wherein
R^2 is pyridazinyl, dihydropyridazinyl, tetrahydropyridazinyl, pyrimidinyl, dihydropyrimidinyl, pyridyl, dihydropyridyl, tetrahydropyridyl, pyrazolyl or imidazothiadiazolyl, each of which may have 1 to 4 suitable substituent(s) selected from a group consisting of lower alkyl which may have 1 to 4 suitable substituent(s) selected from a group consisting of hydroxy, halogen, lower alkoxy and an acyl group; carboxy(lower)-alkenyl; amino; di(lower)alkylamino; halogen; lower alkoxy; oxo; hydroxy; cyano and an acyl group.

5. A compound of claim 4, wherein
R^2 is pyridazinyl, dihydropyridazinyl, tetrahydropyridazinyl, pyrimidinyl, dihydropyrimidinyl, pyridyl, dihydropyridyl, tetrahydropyridyl, pyrazolyl or imidazothiadiazolyl, each of which may have 1 to 4 suitable substituent(s) selected from a group consisting of lower alkyl, lower alkyl having hydroxy and halogen, hydroxy(lower)alkyl, lower alkoxy(lower)alkyl, carboxy(lower)alkyl, protected carboxy-lower)alkyl, carboxy-(lower)alkenyl, amino, di(lower)alkylamino, halogen, lower alkoxy, oxo, hydroxy, cyano, carboxy, protected carboxy and lower alkanoyl.

6. A compound of claim 5, wherein
R^2 is pyridazinyl, dihydropyridazinyl or tetrahydropyridazinyl, each of which may have 1 or 2 suitable substituent(s) selected from a group consisting of lower alkyl, lower alkyl having hydroxy and halogen, hydroxy(lower)alkyl, lower alkoxy(lower)alkyl, carboxy-lower)alkyl, esterified carboxy(lower)alkyl, amidated carboxy(lower)alkyl, carboxy(lower)alkenyl, di(lower)alkylamino, halogen, lower alkoxy, oxo and esterified carboxy.

7. A compound of claim 6, wherein
R^2 is pyridazinyl which may have 1 suitable substituent selected from a group consisting of lower alkyl, lower alkyl having hydroxy and halogen, carboxy(lower)alkenyl, di(lower)alkylamino, halogen and lower alkoxy.

8. A compound of claim 6, wherein
R^2 is dihydropyridazinyl which may have 1 or 2 suitable substituent(s) selected from a group consisting of lower alkyl, hydroxy(lower)alkyl, lower alkoxy(lower)alkyl, carboxy(lower)alkyl, lower alkoxycarbonyl(lower)-alkyl, carbamoyl(lower)alkyl, N,N-di(lower)alkylcarbamoyl(lower)alkyl wherein two lower alkyl groups on nitrogen atom may bond to each other to form 3 to 6-membered ring, halogen, oxo and lower alkoxycar-bonyl.

9. A compound of claim 8, wherein
R^2 is 3-oxo-2,3-dihydropyridazinyl which may have 1 suitable substituent selected from a group consisting of lower alkyl, hydroxy(lower)alkyl, lower alkoxy(lower)alkyl, carboxy(lower)alkyl, lower alkoxycarbonyl-(lower)alkyl, carbamoyl(lower)alkyl and N,N-di(lower)alkylcarbamoyl(lower)alkyl wherein two lower alkyl groups on nitrogen atom may bond to each other to form 3 to 6-membered ring.

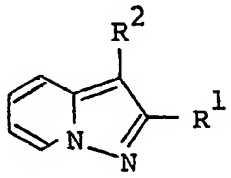
10. A compound of claim 9, wherein
R^2 is 3-oxo-2,3-dihydropyridazinyl which may have carboxy-lower)alkyl.

11. A compound of claim 10, which is selected from a compound consisting of :
3-[2-(2-carboxyethyl)-3-oxo-2,3-dihydropyridazin-6-yl]-2-phenylpyrazolo[1,5-a]pyridine,
3-[2-(3-carboxypropyl)-3-oxo-2,3-dihydropyridazin-6-yl]-2-phenylpyrazolo[1,5-a]pyridine, and
3-[2-(4-carboxybutyl)-3-oxo-2,3-dihydropyridazin-6-yl]-2-phenylpyrazolo[1,5-a]pyridine.

12. A compound of claim 6, wherein
R^2 is tetrahydropyridazinyl which may have 1 or 2 suitable substituent(s) selected from a group consisting of carboxy(lower)alkyl, lower alkoxycarbonyl(lower)alkyl and oxo.

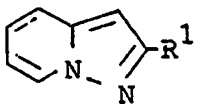
13. A compound of claim 5, wherein
R^2 is pyrimidinyl which may have 1 suitable substituent selected from a group consisting of lower alkyl, amino, halogen and lower alkoxy;
dihydropyrimidinyl which may have 1 or 2 suitable substituent(s) selected from a group consisting of lower alkoxycarbonyl(lower)alkyl and oxo;
pyridyl which may have 1 suitable substituent selected from a group consisting of halogen, lower alkoxy, cyano and lower alkanoyl;
dihydropyridyl which may have 1 to 4 suitable substituent(s) selected from a group consisting of lower alkyl, carboxy(lower)alkyl, lower alkoxycarbonyl(lower)alkyl, oxo, cyano, carboxy, lower alkoxycarbonyl and lower alkanoyl; tetrahydropyridyl which may have 1 or 2 suitable substituent(s) selected from a group consisting of carboxy(lower)alkyl, lower alkoxycarbonyl(lower)alkyl and oxo;
pyrazolyl which may have 1 or 2 suitable substituent(s) selected from a group consisting of lower alkyl, carboxy(lower)alkyl, lower alkoxycarbonyl(lower)alkyl and hydroxy; and
imidazothiadiazolyl which may have lower alkyl.

14. A process for preparing a pyrazolopyridine compound of the formula :



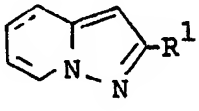
wherein
R^1 is aryl, and
R^2 is unsaturated heterocyclic group which may have one or more suitable substituent(s),
or a salt thereof, which comprises

1) reacting a compound of the formula :

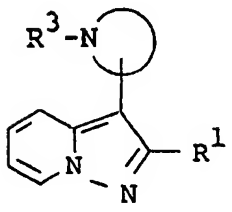


wherein R^1 is as defined above,
or a salt thereof, with a compound of the formula :
R^2_a
wherein R^2_a is heterocyclic compound having
O
‖
- C - moiety in its ring, which may have one or more suitable substituent(s),
or a salt thereof, or

2) reacting a compound of the formula :



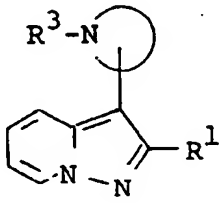
wherein R^1 is as defined above,
or a salt thereof, with a compound of the formula :
R^2_b
wherein R^2_b is N-containing unsaturated heterocyclic compound having =N- moiety in its ring, which may have one or more suitable substituent(s),
or a salt thereof, to give a compound of the formula:



wherein
R^1 is as defined above,
R^3 is an acyl group, and a group of the formula :

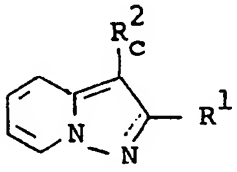
is unsaturated cyclic amino group, which may have one or more suitable substituent(s),
or a salt thereof, or

3) subjecting a compound of the formula :



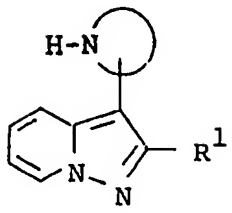
wherein R^1, R^3 and a group of the formula :

are each as defined above,
or a salt thereof, to removal reaction of an acyl group, to give a compound of the formula :



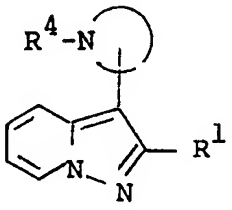
wherein
R^1 is as defined above, and
R^2_c is N-containing unsaturated heterocyclic group, which may have one or more suitable substituent(s),
or a salt thereof, or

4) subjecting a compound of the formula :



wherein R^1 and a group of the formula :

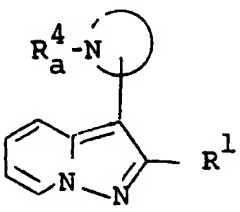
are each as defined above, or a salt thereof,
to introduction reaction of lower alkyl which may have one or more suitable substituent(s), to give a compound of the formula :



wherein
R^1 and a group of the formula :

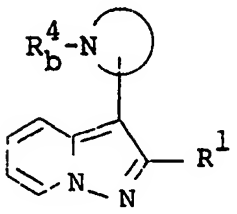
are each as defined above, and
R^4 is lower alkyl which may have one or more suitable substituent(s),
or a salt thereof, or

5) subjecting a compound of the formula :



wherein
R^1 and a group of the formula :

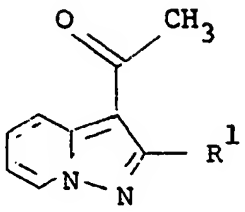
are each as defined above, and
R_a^4 is protected carboxy-lower)alkyl, or a salt thereof, to removal reaction of carboxy protective group, to give a compound of the formula :



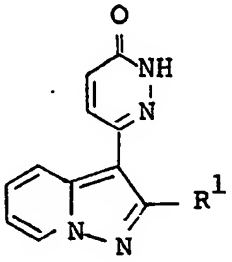
wherein
R^1 and a group of the formula :

are each as defined above, and
R_b^4 is carboxy(lower)alkyl, or a salt thereof, or

6) subjecting a compound of the formula :

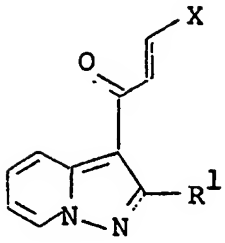


wherein R^1 is as defined above,
or a salt thereof, to formation reaction of pyridazinone group, to give a compound of the formula :

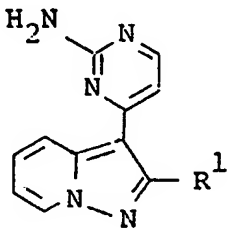


wherein R^1 is as defined above,
or a salt thereof, or

7) reacting a compound of the formula :

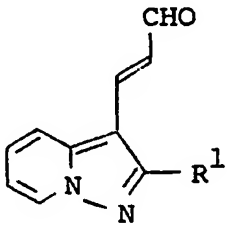


wherein
R^1 is as defined above, and
X is a leaving group,
or a salt thereof, with a compound of the formula :
$HN=C(NH_2)_2$ or a salt thereof, to give a compound of the formula:

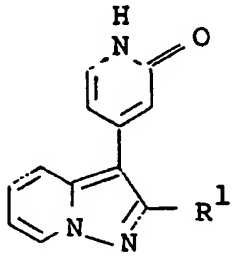


wherein R^1 is as defined above,
or a salt thereof, or

8) reacting a compound of the formula :

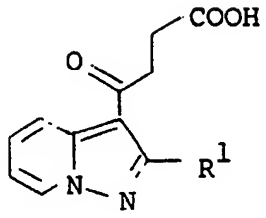


wherein R^1 is as defined above,
or a salt thereof, with a compound of the formula :
CH_3CONH_2
or its reactive derivative at methyl group or a salt thereof, to give a compound of the formula:

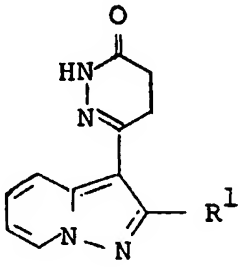


wherein R^1 is as defined above,
or a salt thereof, or

9) reacting a compound of the formula :

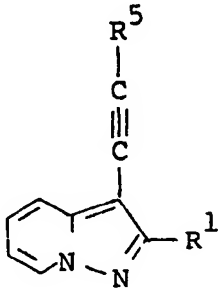


wherein R^1 is as defined above,
or a salt thereof, with a compound of the formula :
$H_2N\text{-}NH_2$
or a salt thereof, to give a compound of the formula:

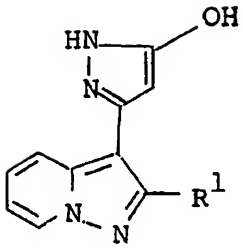


wherein R^1 is as defined above,
or a salt thereof, or

10) reacting a compound of the formula :

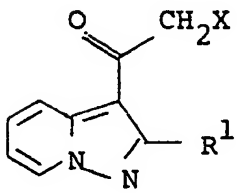


wherein
R^1 is as defined above, and
R^5 is protected carboxy,
or a salt thereof, with a compound of the formula :
$H_2N\text{-}NH_2$
or a salt thereof, to give a compound of the formula:

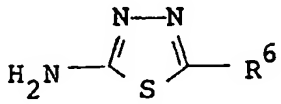


wherein R^1 is as defined above,
or a salt thereof, or

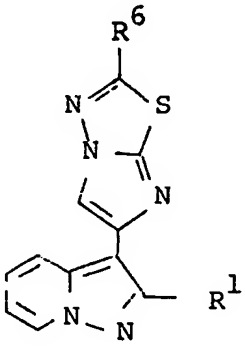
11) reacting a compound of the formula :



wherein R^1 and X are each as defined above,
or a salt thereof, with a compound of the formula :

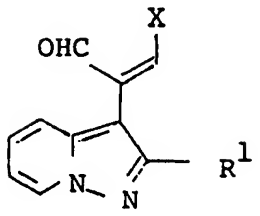


wherein R^6 is lower alkyl,
or a salt thereof, to give a compound of the formula:

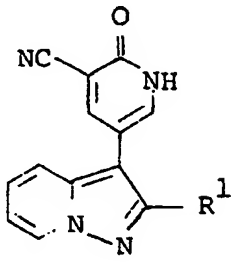


wherein R^1 and R^6 are each as defined above,
or a salt thereof, or

12) reacting a compound of the formula :

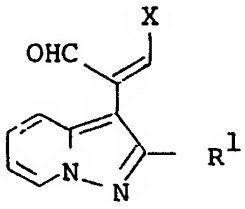


wherein R^1 and X are each as defined above,
or a salt thereof, with a compound of the formula :
$NC\text{-}CH_2CONH_2$
or a salt thereof, to give a compound of the formula:

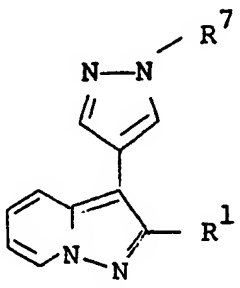


wherein R^1 is as defined above,
or a salt thereof, or

13) reacting a compound of the formula :

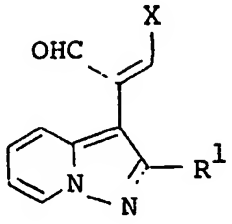


wherein R^1 and X are each as defined above,
or a salt thereof, with a compound of the formula :
$H_2N\text{-}NHR^7$
wherein R^7 is hydrogen or lower alkyl,
or a salt thereof, to give a compound of the formula:

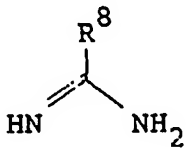


wherein R^1 and R^7 are each as defined above,
or a salt thereof, or

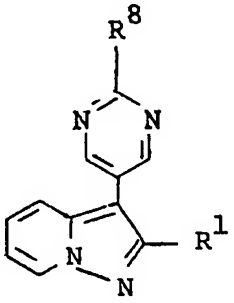
14) reacting a compound of the formula :



wherein R^1 and X are each as defined above,
or a salt thereof, with a compound of the formula :

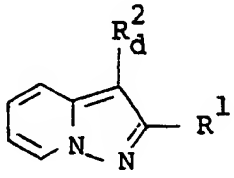


wherein R^8 is hydrogen, lower alkyl or amino,
or a salt thereof, to give a compound of the formula:

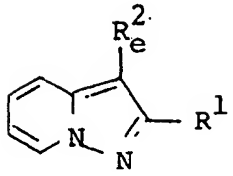


wherein R^1 and R^8 are each as defined above,
or a salt thereof, or

15) subjecting a compound of the formula :

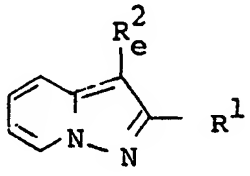


wherein
R^1 is as defined above,
R^2_d is unsaturated heterocyclic group having cyano, which may have one or more suitable substituent(s),
or a salt thereof, to hydrolysis reaction of cyano group, to give a compound of the formula :

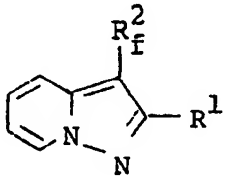


wherein
R^1 is as defined above,
R_e^2 is unsaturated heterocyclic group having carboxy, which may have one or more suitable substituent(s),
or a salt thereof, or

16) subjecting a compound of the formula :

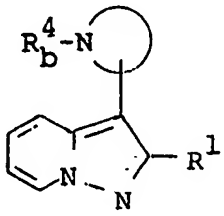


wherein R^1 and R_e^2 are each as defined above,
or a salt thereof, to removal reaction of carboxy group, to give a compound of the formula :



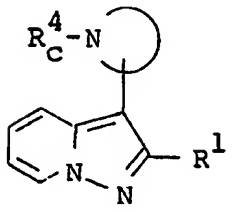
wherein
R^1 is as defined above,
R_f^2 is unsaturated heterocyclic group which may have one or more suitable substituent(s) except carboxy,
or a salt thereof, or

17) subjecting a compound of the formula :



wherein R^1, R_b^4 and a group of the formula :

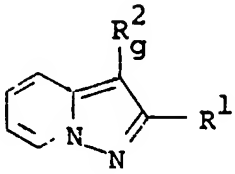
are each as defined above,
or a salt thereof, to amidation reaction, to give a compound of the formula :



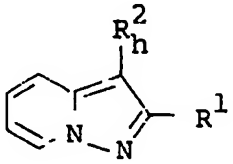
wherein
R^1 and a group of the formula :

are each as defined above, and
R_c^4 is amidated carboxy-lower)alkyl, or a salt thereof, or

18) subjecting a compound of the formula :

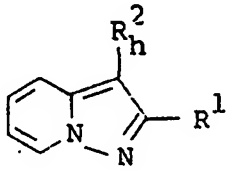


wherein
R^1 is as defined above,
R_g^2 is unsaturated heterocyclic group having amino, which may have one or more suitable substituent(s), or a salt thereof, to conversion reaction of amino group to oxo group, to give a compound of the formula :



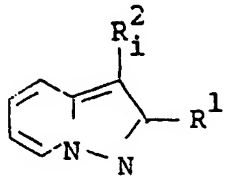
wherein
R^1 is as defined above,
R_h^2 is unsaturated heterocyclic group having oxo, which may have one or more suitable substituent(s), or a salt thereof, or

19) subjecting a compound of the formula :



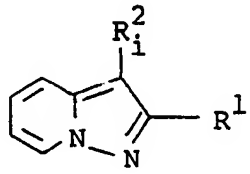
wherein R^1 and R_h^2 are each as defined above,

or a salt thereof, to halogenation reaction, to give a compound of the formula :

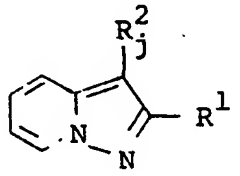


wherein
R^1 is as defined above,
R_i^2 is unsaturated heterocyclic group having halogen, which may have one or more suitable substituent(s),
or a salt thereof, or

20) reacting a compound of the formula :

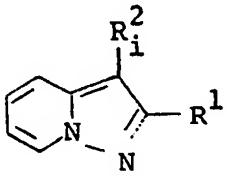


wherein R^1 and R_i^2 are each as defined above,
or a salt thereof, with di(lower)alkylamine, or a salt thereof, to give a compound of the formula:

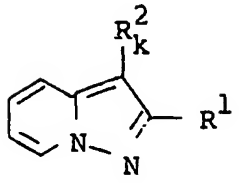


wherein
R^1 is as defined above,
R_j^2 is unsaturated heterocyclic group having di(lower)alkylamino, which may have one or more suitable substituent(s),
or a salt thereof, or

21) subjecting a compound of the formula :

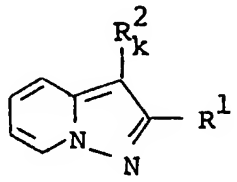


wherein R^1 and R_i^2 are each as defined above,
or a salt thereof, to conversion reaction of halogen to lower alkoxy, to give a compound of the formula :

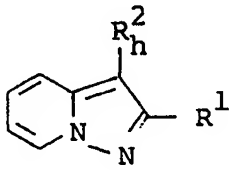


wherein
R^1 is as defined above,
R^2_k is unsaturated heterocyclic group having lower alkoxy, which may have one or more suitable substituent-(s),
or a salt thereof, or

22) subjecting a compound of the formula :

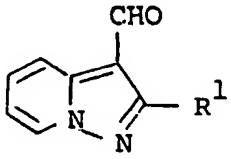


wherein R^1 and R^2_k are each as defined above,
or a salt thereof, to conversion reaction of lower alkoxy to oxo group, to give a compound of the formula :



wherein R^1 and R^2_h are each as defined above,
or a salt thereof, or

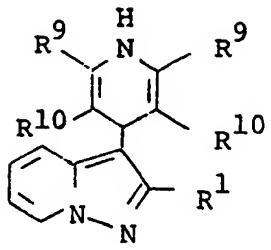
23) reacting a compound of the formula :



wherein R^1 is as defined above,
or a salt thereof, with a compound of the formula :

R^9-C(=O)-CH_2-R^{10}

wherein
R^9 is lower alkyl, and
R^{10} is protected carboxy,
and ammonia, to give a compound of the formula :



wherein R^1, R^9 and R^{10} are each as defined above,
or a salt thereof.

15. A pharmaceutical composition which comprises, as an active ingredient, a compound of claim 1 or a pharmaceutically acceptable salt thereof in admixture with pharmaceutically acceptable carriers.

16. A compound of claim 1 or a pharmaceutically acceptable salt thereof for use as a medicament.

17. A compound of claim 1 or pharmaceutically acceptable salts thereof for use in treating or preventing melancholia, heart failure, hypertension, renal insufficiency, edema, obesity, bronchial asthma, gout, hyperuricemica, sudden infant death syndrome, immunosuppresion, diabetes, myocardiac infarction, thrombosis, obstruction, arteriosclerosis obliterans, thrombophlebitis, cerebral infarction, transient ischemi attack or angina pectoris.

18. Use of a compound of claim 1 or pharmaceutically acceptable salts thereof for the manufacture of a medicament for therapeutic treatment of melancholia, heart failure, hypertension, renal insufficiency, edema, obesity, bronchial asthma, gout, hyperuricemia, sudden infant death syndrome, immunosuppresion, diabetes, myocardiac infarction, thrombosis, obstruction, arteriosclerosis obliterans, thrombophlebitis, cerebral infarction, transient ischemic attack or angina pectoris.

European Patent Office

EUROPEAN SEARCH REPORT

Application Number

EP 90 10 1042

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.5)
A	EP-A-0 299 209 (FUJISAWA PHARMACEUTICAL CO. LTD) * claims 1,23-25 * ---	1,15-18	C 07 D 471/04 A 61 K 31/44 // (C 07 D 471/04 C 07 D 231:00 C 07 D 221:00)
A	EP-A-0 270 926 (KYORIN SEIYAKU K.K.) * abstract; page 7, lines 18-23 * ---	1,15,16	
A	BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN vol. 61, 1988, pages 2055-2061; Tokyo, JP; A. KAKEHI et al.: "Preparation of New Nitrogen-Bridged Heterocycles. 18. Facile Formations of 3-Arylpyrazolo (1,5-alpyridines and 1-Arylindolizines" * page 2056, scheme 1, products no. 4f and 41 * ---	1	
A	CHEMICAL ABSTRACTS vol. 104, no. 23, 9th June 1986, page 756, abstract no. 207259c, Columbus, Ohio, US; & JP - A - 60 248 689 (MITSUBISHI PAPER MILLS LTD.) 09.12.1985 ---	14	TECHNICAL FIELDS SEARCHED (Int. Cl.5) C 07 D 471/00
A	DE-A-2 546 196 (KYORIN PHARMACEUTICAL CO. LTD.) * claim 1 * -----	14	

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
BERLIN	11-04-1990	HASS C V F

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

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